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(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
30 January 2003 (30.01.2003)

PCT

(10) International Publication Number
WO 03/008389 A1

(51) International Patent Classification[7]: C07D 241/02, 243/08, 263/04, 413/14, A61K 31/55, 31/535, 31/495, 31/50, 31/445, 31/42, A61P 31/00

(21) International Application Number: PCT/IB02/00167

(22) International Filing Date: 18 January 2002 (18.01.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PCT/IB01/01262 16 July 2001 (16.07.2001) IB

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(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/008389 A1

(54) Title: OXAZOLIDINONE DERIVATIVES AS POTENTIAL ANTIMICROBIALS

(57) Abstract: The present invention relates to certain substituted phenyl oxazolidinones and to processes for the synthesis of the same. This invention also relates to pharmaceutical compositions containing the compounds of the present invention as antimicrobials. The compounds are useful antimicrobial agents, effective against a number of human and veterinary pathogens, including gram-positive aerobic bacteria such as multiply-resistant staphylococci, streptococci and enterococci as well as anaerobic organisms such as Bacteroides spp. and Clostridium spp. species, and acid fast organisms such as Mycobacterium tuberculosis, Mycobacterium avium and Mycobacterium spp.

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OXAZOLIDINONE DERIVATIVES AS POTENTIAL ANTIMICROBIALS

Field of the Invention

The present invention relates to certain substituted phenyl oxazolidinones and to processes for the synthesis of the same. This invention also relates to pharmaceutical compositions containing the compounds of the present invention as antimicrobials. The compounds are useful antimicrobial agents, effective against a number of human and veterinary pathogens, including gram-positive aerobic bacteria such as multiply-resistant staphylococci, streptococci and enterococci as well as anaerobic organisms such as *Bacteroides* spp. and *Clostridium* spp. species, and acid fast organisms such as *Mycobacterium tuberculosis*, *Mycobacterium avium* and *Mycobacterium* spp.

Background of the Invention

Increasing antibacterial resistance in gram positive bacteria has presented a formidable treatment problem. The *enterococci*, although traditionally non virulent pathogens, have been shown, when associated with Vancomycin resistance, to have an attributable mortality of approximately 40%. *Staphylococcus aureus*, the traditional pathogen of post operative wounds, has been resistant to Penicillin due to production of penicillinases. This resistance was overcome by the development of various penicillinase stable β lactams. But the pathogen responded by synthesizing a modified target penicillin binding protein- 2' leading to less affinity for β lactam antibiotics and a phenotype known as Methicillin Resistant *S. aureus* (MRSA). These strains, till recently were susceptible to Vancomycin, which inspite of its various drawbacks, has become the drug of choice for MRSA infections. *Streptococcus pneumoniae* is a major pathogen causing pneumonia, sinusitis and meningitis. Until very recently it was highly susceptible to penicillin. Recently though, different PBP 2' strains with different susceptibility to penicillin have been reported from across the globe.

Oxazolidinones are a new class of synthetic antimicrobial agents which kill Gram positive pathogens by inhibiting a very early stage of protein synthesis. Oxazolidinones inhibit the formation of ribosomal initiation complex involving 30S

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and 50S ribosomes leading to prevention of initiation complex formation. Due to their novel mechanism of action, these compounds are active against pathogens resistant to other clinically useful antibiotics.

WO93/23384 application discloses phenyloxazolidinones containing a substituted diazine moiety and their uses as antimicrobials.

WO93/09103 application discloses substituted aryl and heteroaryl- phenyl-oxazolidinones useful as antibacterial agents.

WO90/02744 application discloses 5-indolinyl-5β-amidomethyloxazolidinones, 3-(fused ring substituted) phenyl-5β-amidomethyloxazolidinones which are useful as antibacterial agents..

European Patent Publication 352,781 discloses phenyl and pyridyl substituted phenyl oxazolidinones.

European Patent Application 312,000 discloses phenylmethyl and pyridinylmethyl substituted phenyl oxazolidinones.

U.S. Patent No. 5,254,577 discloses nitrogen heteroaromatic rings attached to phenyloxazolidinone.

U.S. Patents No. 5,547,950 and 5,700,799 also disclose the phenyl piperazinyl oxazolidinones.

Other references disclosing various phenyloxazolidinones include U.S. Patents No. 4,801,600 and 4,921,869; Gregory W.A., *et al.*, *J.Med.Chem.*, 32, 1673-81 (1989); Gregory W.A., *et al.*, *J.Med.Chem.*, 33, 2569-78 (1990); Wang C., *et al.*, *Tetrahedron*, 45, 1323-26 (1989); Brittelli, *et al.*, *J.Med. Chem.*, 35, 1156 (1992); and *Bio-organic and Medicinal Chemistry Letters*, 9, pp. 2679-2684, 1999; Antibacterial & Antifungal Drug Discovery & Development Summit, Strategic Research Institute, June 28-29, 2001, Amsterdam, The Netherlands; Posters No. 1822, 1823, 1824, 1825, 1826, 1827, 1828, 1829, 1830, 1831, 1832, 1833, and 1834, 40th Interscience Conference on Antimicrobial Agents and Chemotherapy, Sept 17-20, 2000, Toronto, Canada.

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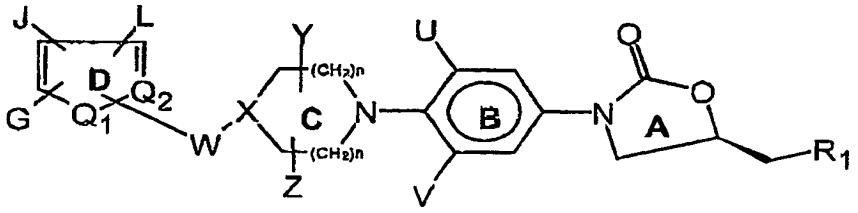
Summary of the Invention

The objective of this invention is to synthesize, identify and profile oxazolidinone molecules which have good activity against multiply resistant gram positive pathogens like MRSA, VRE and PRSP. Some of these molecules have activity against MDR-TB and MAI strains, while others have significant activity against important anaerobic bacteria.

The compounds of the present invention are related by their substituted phenyloxazolidinone ring structure in the compounds disclosed to the publications described above except that the subject compounds have a diazine moiety attached to the phenyloxazolidinone which is further substituted by heterocyclic, aryl, substituted aryl, heteroaroamatic ring therefore the compounds are unique and have superior antibacterial activity.

Another object of the present invention is to provide processes for the novel phenyloxazolidinones derivatives that exhibit significantly greater antibacterial activity, than available with the present compounds against multiply resistant gram positive pathogens like MRSA, VRE and PRSP , MDR-TB and MAI strains, in order to provide safe and effective treatment of bacterial infections.

In order to achieve the above-mentioned objectives and in accordance with the purpose of the invention as embodied and broadly described herein, there is provided a process for the synthesis of novel phenyloxazolidinone derivatives represented by Formula I,



Formula I

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wherein

ring C is four to eight membered in size or larger which has either two or three carbon atoms between each nitrogen atoms or ring C is a bridged bicyclic system and is optionally substituted by the substituents Y and Z independently selected from alkyl groups, cycloakyl groups, fluoro group, carboxylic groups and corresponding esters or amides;

D is a five membered heterocyclic ring; the preferred heterocyclic rings are furanyl,thienyl,pyrrolyl and pyrazolyl;

Q_1 is selected from O, S, NR_{11};

Q_2 is selected from N or C;

G, J, L are independently selected from H, C_{1-6} alkyl, F, Cl, Br,I, –CN, COR_5,$COOR_5$, $N(R_6,R_7)$, $NHCOC(R_8, R_9)$,-$NHCOOR_5$,CON (R_6, R_7), CH_2NO_2, NO_2, CH_2R_8, CHR_9, -CH = N-OR_{10}, -C=CH-R_5, OR_5, SR_5, -$C(R_9)=C(R_9)NO_2$, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I, OR_4, SR_4; wherein R_5 is selected from H, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted with one or more of F, Cl, Br, I or OH, aryl, heteroaryl; R_6 and R_7, are independently selected from H, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy; R_8 and R_9 are independently selected from H, C_{1-6} alkyl, F, Cl, Br, I, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I, OR_5, SR_4, $N(R_6,R_7)$;, R_{10}= H, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, aryl, heteroaryl; except when W is C=O, Q_1=S, Q_2=C, and G, J, L=H;

R_1 is selected from the group consisting of - $NHC(=O)R_2$, $N(R_3, R_4)$, -$NR_2C(=S)R_3$, -$NR_2C(=S)SR_3$, wherein R_2 is hydrogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted with one or more of F, Cl, Br, I or OH; R_3,R_4 are independently selected from hydrogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted with one or more of F, Cl, Br, I or OH; preferably R_1 is of the formula –NH(C=O)X wherein X is CH_3, CH_2F, CHF_2, CF_3, CH_2Cl. $CHCl_2$, CCl_3;

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U and V are independently selected from hydrogen, optionally substituted C_{1-6} alkyl, F, Cl, Br, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I, preferably U and V are hydrogen or fluoro;

X is selected from C, CH, CH-S, CH-O and N;

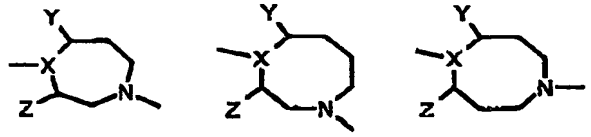
Y and Z are independently selected from hydrogen, C_{1-6} alkyl, C_{3-12} cycloalkyl and C_{0-3} bridging groups;

W is selected from the group CH_2, CO, CH_2NH, $-NHCH_2$, $-CH_2NHCH_2$, $-CH_2-N(R_{11})CH_2-$, $CH_2(R_{11})N-$, $CH(R_{11})$, S, $CH_2(CO)$, NH, O, $N(R_{11})$, $(CO)CH_2$, $N(R_{11})CON(R_{11})$, $N(R_{11})C(=S)N(R_{11})$, SO_2, SO, wherein R_{11} is hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl, heteroaryl; and,

n is an integer in the range from 0 to 3.

Preferred compounds of Formula I have R_1 as acetamide or halogen substituted acetamide and the most preferred compounds in this series would be prepared as the optically pure enantiomers having the (S)-configuration according to the Cahn-Ingold-Prelog notation at C_5 of the oxazolidinone ring. The (S)-enantiomer of this series of compounds is preferred since it has two times more antibacterial activity than the corresponding racemic compound. The scope of the individual isomers and mixture of enantiomers of the structural Formula I are also covered in this invention.

In the more preferred compounds represented by Formula I ring C may be four to eight membered in size and the larger rings may have either two or three carbons between each nitrogen atom, for example:



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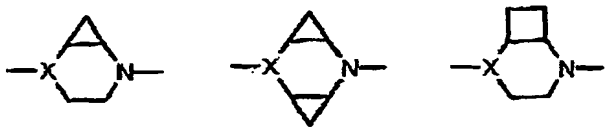
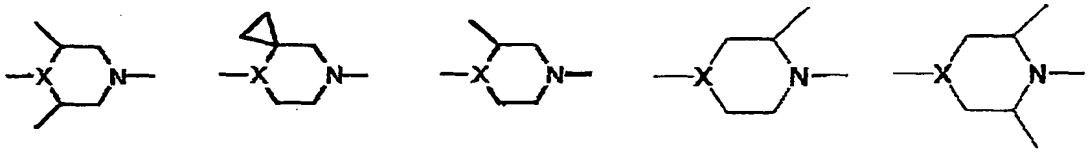
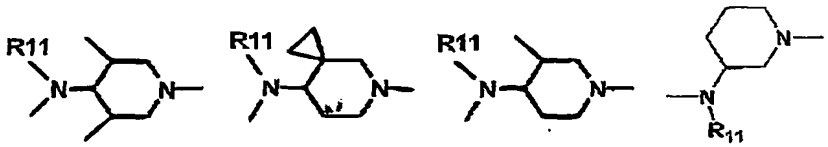
The ring C may be bridged to form a bicyclic system as shown below:

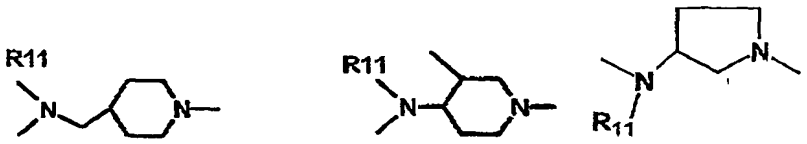


Ring C is optionally substituted by Y and Z with alkyl groups, cycloalkyl groups, fluoro group, carboxylic and corresponding esters, amides, substituted alkyls or bridging alkyl groups are as shown below:



When ring C is five or six membered in size and X is -CH-(NHR), or $>CCH_2NHR$-, the following rings are preferred ones wherein R_{11} is the same as defined earlier.





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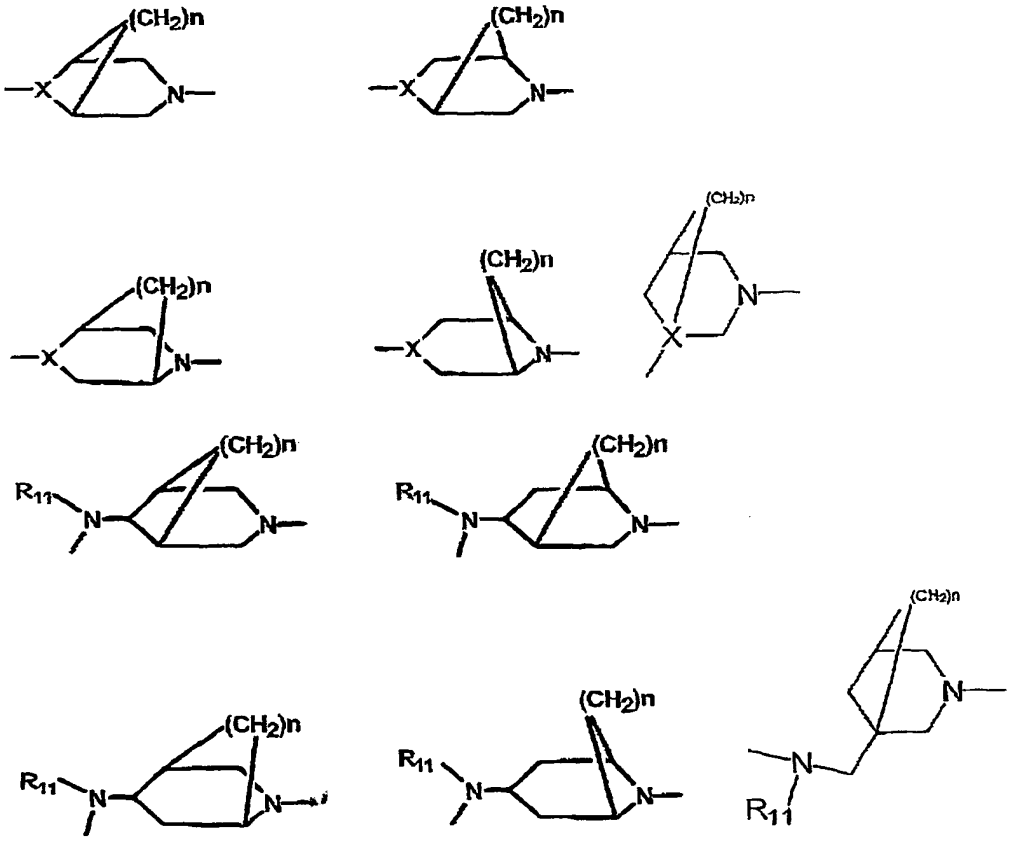
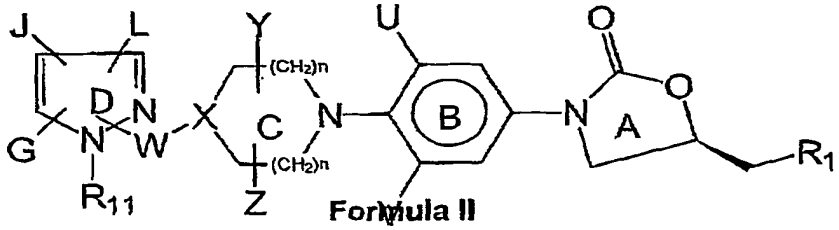
In addition to the above, ring C also includes the following structures:



Still more preferred compounds of Formula I when Q_1 = NR_{11}, and Q_2 = N is represented by Formula II wherein rings C and D are the same as defined before;



Formula II

R_1 is selected from the group consisting of –NHC(=O)R_2; -N(R_3, R_4); –$NR_2C(=S)R_3$; -$NR_2C(=S)SR_3$ wherein R_2, R_3, R_4 are independently hydrogen,

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C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted with one or more of F, Cl, Br, I, OH; preferably R_1 is of the formula –NH(C=O)X wherein X is CH_3, CH_2F, CHF_2, CF_3, CH_2Cl. $CHCl_2$, CCl_3;

U and **V** are independently selected from hydrogen, optionally substituted C_{1-6} alkyl, F, Cl, Br, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I; preferably U and V are hydrogen or fluoro;

Y and **Z** are independently selected from hydrogen, C_{1-6} alkyl, C_{3-12} cycloalkyl C_{0-3} bridging group;

X is selected from C, CH, CH-S, CH-O, and N;

W is independently selected from the group CH_2, CO, CH_2NH, -$NHCH_2$, -CH_2NHCH_2, -CH_2-N (R_{11}) CH_2 -, CH_2 (R_{11}) N -, CH (R_{11}), S, CH_2(CO), NH, O, N(R_{11}), (CO)CH_2, N(R_{11})CON(R_{11}), N(R_{11})C(=S)N(R_{11}), SO_2, SO, wherein R_{11} is hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl, heteroaryl;

G, J, L are independently selected from H, C_{1-6} alkyl, F, Cl, Br,I, –CN, COR_5,$COOR_5$, N(R_6,R_7), NHCOC(R8, R9), $NHCOOR_5$,CON (R_6, R_7), CH_2NO_2, NO_2, CH_2R_8, CHR_9, -CH = N-OR_{10}, -C=CH-R_5, OR_5, SR_5, -C(R_9)=C(R_9)NO_2, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I, OR_4, SR_4; wherein R_5 is selected from H, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted with one or more F, Cl, Br, I or OH, aryl, heteroaryl; R_6 and R_7, are independently selected from H, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy; R_8 and R_9 are independently selected from H, C_{1-6} alkyl, F, Cl, Br, I, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I, OR_5, SR_4, N(R_6,R_7);, R_{10}= H, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, aryl, heteroaryl;

n is an integer in the range from 0 to 3;

more preferred G, J and L substitutions are nitro, aldehydes and halides;

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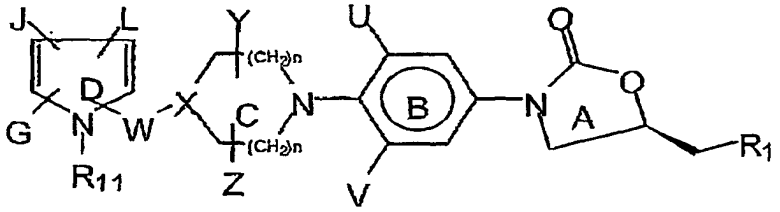
preferably W is selected from the groups consisting of CH_2, C(=O), C(=O)-C(=O), CH_2NH, $-NHCH_2$, $-CH_2NHCH_2$, $-CH_2-N(CH_3)CH_2-$, CH_2 (CH_3)N -, CH (CH_3), S and CH_2(C=O), -NH. The preferred compounds of Formula II are as follows:

(S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-pyrazolecarbonyl-(4-nitro)}]piperazinyl] phenyl-]-2-oxo-5-oxazolidinyl[methyl]acetamide

(S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-pyrazolecarbonyl-(5-nitro)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide

Still more preferred compounds of Formula I when Q_1 = NR_{11}, and Q_2 = carbon is represented by Formula III



Formula III

wherein

rings C and D are the same as defined before;

R_1 is selected from the group consisting of $-NHC(=O)R_2$; $-N(R_3, R_4)$; $-NR_2C(=S)R_3$; $-NR_2C(=S)SR_3$ wherein R_2, R_3, R_4 are independently hydrogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted one or more F, Cl, Br, I, OH; preferably R_1 is of the formula $-NH(C=O)X$ wherein X is CH_3, CH_2F, CHF_2, CF_3, CH_2Cl. $CHCl_2$, CCl_3;

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U and **V** are independently selected from hydrogen, optionally substituted C_{1-6} alkyl, F, Cl, Br, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I; preferably U and V are hydrogen and fluoro;

Y and **Z** are independently selected from hydrogen, C_{1-6} alkyl, C_{3-12} cycloalkyl , C_{0-3} bridging group.

X is selected from C, CH, CH-S, CH-O, and N;

W is independently selected from CH_2, CO, CH_2NH, $-NHCH_2$, $-CH_2NHCH_2$, $-CH_2-N(R_{11})CH_2-$, $CH_2(R_{11})N-$, $CH(R_{11})$, S, $CH_2(CO)$, NH, O, $N(R_{11})$, $(CO)CH_2$, $N(R_{11})CON(R_{11})$, $N(R_{11})C(=S)N(R_{11})$, SO_2, SO, wherein R_{11} is hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl, heteroaryl;

G, J, L are independently selected from H, C_{1-6} alkyl, F, Cl, Br,I, –CN, COR_5,$COOR_5$, $N(R_6,R_7)$, $NHCOC(R_8, R_9)$, $NHCOOR_5$,CON (R_6, R_7), CH_2NO_2, NO_2, CH_2R_8, CHR_9, $-CH=N-OR_{10}$, $-C=CH-R_5$, OR_5, SR_5, $-C(R_9)=C(R_9)NO_2$, C_{1-12} alkyl substituted with one or more F, Cl, Br, I, OR_4, SR_4; wherein R_5 is selected from H, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted with one or more F, Cl, Br, I or OH, aryl, heteroaryl; R_6 and R_7, are independently selected from H, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy; R_8 and R_9 are independently selected from H, C_{1-6} alkyl, F, Cl, Br, I, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I, OR_5, SR_4, $N(R_6,R_7)$;, R_{10}= H, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, aryl, heteroaryl;

n is an integer in the range from 0 to 3;

more preferred G, J and L substitutions are nitro, aldehydes and halides.

Preferably W is selected from the groups consisting of CH_2, C(=O), C(=O)-C(=O), CH_2NH, $-NHCH_2$, $-CH_2NHCH_2$, $-CH_2-N(CH_3)CH_2-$, $CH_2(CH_3)N-$, CH (

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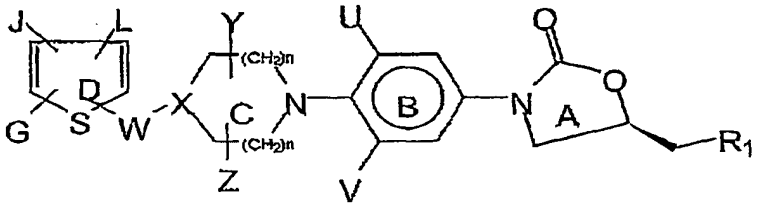
CH_3), S and CH_2(C=O), -NH. The preferred compounds of Formula III are as follows:

(S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-pyrrole-(1-methyl-5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide

(S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-pyrrole-(5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl] acetamide

Still more preferred compounds of Formula I is represented by Formula IV with Q_1 = sulphur and Q_2 = carbon of Formula I,



Formula IV

wherein

rings C and D are the same as defined before;

R_1 is selected from the group consisting of $-NHC(=O)R_2$, $-N(R_3, R_4)$, $-NR_2C(=S)R_3$, $-NR_2C(=S)SR_3$ wherein R_2, R_3, R_4 are independently hydrogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted one or more of F, Cl, Br, I, OH; preferably R_1 is of the formula $-NH(C=O)X$ wherein X is CH_3, CH_2F, CHF_2, CF_3, CH_2Cl. $CHCl_2$, CCl_3;

U and V are independently selected from hydrogen, optionally substituted C_{1-6} alkyl, F, Cl, Br, C_{1-12} alkyl substituted with one or more F, Cl, Br, I; preferably U and V are hydrogen and fluoro;

Y and Z are independently selected from hydrogen, C_{1-6} alkyl, C_{3-12} cycloalkyl C_{0-3} bridging group;

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X is selected from C, CH, CH-S, CH-O, and N;

W is independently selected from CH_2, CO, CH_2NH, -$NHCH_2$, -CH_2NHCH_2, -CH_2-N (R_{11}) CH_2-, CH_2 (R_{11}) N -, CH (R_{11}), S, CH_2(CO), NH, O, N(R_{11}), (CO)CH_2, N(R_{11})CON(R_{11}), N(R_{11})C(=S)N(R_{11}), SO_2, SO, wherein R_{11} is hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl, heteroaryl;

G, J, L are independently selected from H, C_{1-6} alkyl, F, Cl, Br,I, –CN, COR_5,$COOR_5$, N(R_6,R_7), NHCOC(R_8, R_9), $NHCOOR_5$,CON (R_6, R_7), CH_2NO_2, NO_2, CH_2R_8, CHR_9, -CH = N-OR_{10}, -C=CH-R_5, OR_5, SR_5, -C(R_9)=C(R_9)NO_2, C_{1-12} alkyl substituted with one or more F, Cl, Br, I, OR_4, SR_4; wherein R_5 is selected from H, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted with one or more of F, Cl, Br, I or OH, aryl, heteroaryl; R_6 and R_7, are independently selected from H, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy; R_8 and R_9 are independently selected from H, C_{1-6} alkyl, F, Cl, Br, I, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I, OR_5, SR_4, N(R_6,R_7);, R_{10} is H, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, aryl, heteroaryl; except when W=(C=O), Q_1=S, Q_2= C, and G, J, L=H;

n is an integer in the range from 0 to 3.

More preferred G, J and L substitutions are nitro, aldehydes and halides.

Preferably W is selected from the groups consisting of CH_2, C(=O), C(=O)-C(=O), CH_2NH, -$NHCH_2$, -CH_2NHCH_2, -CH_2-N(CH_3)CH_2-, CH_2 (CH_3)N -, CH (CH_3), S and CH_2(C=O), -NH. The preferred compounds of Formula IV are as follows:

(S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen-(4-nitro-)methyl-}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide

(S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(5-nitro)}] homopiperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide

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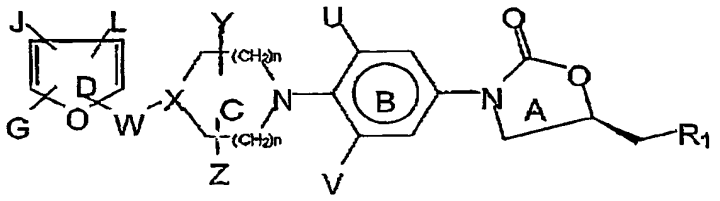
(S)-N-[[3-[3-Fluoro-4-[N-1-[4-[1-{2-thiophenyl-(5-nitro)}-1-ethyl]]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide

(S)-N-[[3-[3-Fluoro-4-[N-1-[2-methyl-4-{2-thiophenoyl-(5-nitro)}]- piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide

(S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-2-thiohenoyl-(5-nitro)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide

(S)-N-[[3-[3-Fluoro-4-[N-1,{3-{[N-methyl)[N-{2-thiophenoyl(5-nitro)}]amino pyrrolidinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide.

Still more preferred compounds of Formula I is represented by Formula V with Q_1 = O, Q_2 =C of Formula II,



Formula V

wherein

rings C and D are the same as defined before;

R_1 is selected from the group consisting of –NHC(=O)R_2, -N(R_3, R_4), -NR_2C (=S)R_3, –NR_2C(=S)SR_3 wherein R_2, R_3, R_4 are independently selected from the group consisting of hydrogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted one or more F, Cl, Br, I, OH; preferably R_1 is of the formula –NH (C=O)X wherein X is CH_3, CH_2F, CHF_2, CF_3, CH_2Cl. $CHCl_2$, CCl_3;

U and **V** are independently selected from hydrogen, optionally substituted C_{1-6} alkyl, F, Cl, Br, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I; preferably U and V are hydrogen and fluoro;

Y and **Z** are independently selected from hydrogen, C_{1-6} alkyl, C_{3-12} cycloalkyl , C_{0-3} bridging group;

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X is selected from C, CH, CH-S, CH-O, and N;

W is independently selected from the group consisting of CH_2, CO, CH_2NH, -$NHCH_2$, -CH_2NHCH_2, -CH_2-N (R_{11}) CH_2-, CH_2 (R_{11}) N -, CH (R_{11}), S, CH_2(CO), NH, O, N(R_{11}), (CO)CH_2, N(R_{11})CON(R_{11}), N(R_{11})C(=S)N(R_{11}), SO_2, SO, wherein R_{11} is hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl, heteroaryl;

G, J, L are independently selected from H, C_{1-6} alkyl, F, Cl, Br,I, –CN, COR_5,$COOR_5$, N(R_6,R_7), NHCOC(R_8, R_9), $NHCOOR_5$,CON (R_6, R_7), CH_2NO_2, NO_2, CH_2R_8, CHR_9, -CH = N-OR_{10}, -C=CH-R_5, OR_5, SR_5, -C(R_9)=C(R_9)NO_2, C_{1-12} alkyl substituted with one or more F, Cl, Br, I, OR_4, SR_4; wherein R_5 is selected from H, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted with one or more of F, Cl, Br, I or OH, aryl, heteroaryl; R_6 and R_7, are independently selected from H, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy; R_8 and R_9 are independently selected from H, C_{1-6} alkyl, F, Cl, Br, I, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I, OR_5, SR_4, N(R_6,R_7);, R_{10}= H, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, aryl, heteroaryl;
n is an integer in the range from 0 to 3.

More preferred G, J and L substitutions are nitro, aldehydes and halides.

Preferably W is selected from the groups consisting of CH_2, C(=O), C(=O)-C(=O), CH_2NH, -$NHCH_2$, -CH_2NHCH_2, -CH_2-N(CH_3)CH_2-, CH_2 (CH_3)N -, CH (CH_3), S and CH_2(C=O), -NH. The preferred compounds of Formula V are as follows:

(S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl-(3-methyl)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

(S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl-(3-methyl-5-nitro)}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

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(S)-N-[[3-[3-Fluoro-4-[N-1-[4-[1-{2-furyl-(5-nitro)}-1-ethyl]]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,

(S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-difluoroacetamide,

(S)-N-[[3-[3-Fluoro-4-[4-{N-2-furyl-(5-nitro)methyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide.

The compounds of the present invention are useful as antimicrobial agents, effective against a number of human and veterinary pathogens, particularly aerobic Gram-positive bacteria, including multiply-antibiotic resistant staphylococci and streptococci, as well as anaerobic organisms such as Mycobacterium tuberculosis and other mycobacterium species.

For preparing pharmaceutical compositions from the compounds described by this invention, inert, pharmaceutically acceptable carriers can be either solid or liquid. Solid form preparations include powders, tablets, dispersible granules, capsules, cachets, suppositories, and ointments. A solid carrier can be one or more substances which may also act as diluents, flavouring agents, solubilizers, lubricants, suspending agents, binders, or tablets disintegrating agents; it can also be as finely divided solid which is in admixture with the finely divided active compound. For the preparation of tablets, the active compound is mixed with carrier having the necessary binding properties in suitable proportions and compacted in the shape and size desired. The powders and tablets preferably contain from about 5 to about 70 percent of the active ingredient. Suitable solid carriers are lactose, pectin, dextrin, starch, gelatin, tragacanth, low melting wax, cocoa butter, and the like. The term "preparation" is intended to include the formulation of the active compound with encapsulating material as carrier providing a capsule in which the active component (with or without other carriers) is surrounded by carrier, which is thus in association with it. Similarly, capsules can be used as solid dosage forms suitable for oral administration.

Liquid form preparations include solutions, suspensions, and emulsions. As an example may be mentioned water or water-propylene glycol solutions for parenteral injection. Such solutions are prepared so as to be acceptable to biological systems (isotonicity, pH, etc.). Liquid preparations can also be

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formulated in solution in aqueous polyethylene glycol solution. Aqueous solutions suitable for oral use can be prepared by dissolving the active component in water and adding suitable colorants, flavours, stabilizing, and thickening agents as desired. Aqueous suspension suitable for oral use can be made by dispersing the finely divided active component in water with viscous material, i.e., natural or synthetic gums, resins, methyl cellulose, sodium carboxymethyl cellulose, and other well-known suspending agents.

Ointment preparations contain heavy metal salts of a compound of Formula I with a physiologically acceptable carrier. The carrier is desirably a conventional water-dispersible hydrophilic or oil-in-water carrier, particularly a conventional semi-soft or cream-like water-dispersible or water soluble, oil-in-water emulsion infected surface with a minimum of discomfort. Suitable compositions may be prepared by merely incorporating or homogeneously admixing finely divided compounds with the hydrophilic carrier or base or ointment.

Preferably, the pharmaceutical preparation is in unit dosage form. In such form, the preparation is subdivided into unit doses containing appropriate quantities of the active component. The unit dosage form can be a packaged preparation, the package containing discrete capsules, powders in vials or ampoules, and ointments capsule, cachet, tablet, gel, or cream itself or it can be the appropriate number of any of these packaged forms.

In order to achieve the above mentioned objects in accordance with the purpose of the invention as embodied and broadly described herein, there are provided processes for the synthesis of compounds of Formulae I, II, III, IV and V. Pharmaceutically acceptable non-toxic acid addition salts of the compounds of the present invention of Formulae I, II, III, IV and V may be formed with inorganic or organic acids, by methods well known in the art.

The present invention also includes within its scope prodrugs of the compounds of Formulae I, II, III , IV and V. In general, such prodrugs will be functional derivatives of these compounds which readily get converted in vivo into defined compounds. Conventional procedures for the selection and preparation of suitable prodrugs are known.

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The invention also includes pharmaceutically acceptable salts, the enantiomers, diastereomers, N-oxides, polymorphs, pharmaceutically acceptable solvates, prodrugs, metabolites in combination with pharmaceutically acceptable carrier and optionally included excipient.

Other objects and advantages of the invention will be set forth in the description which follows, and in part will be apparent from the description, or may be learned by the practice of the invention. The objects and the advantages of the invention may be realized and obtained by means of the mechanism and combination pointed out in the appended claims.

Detailed Description of the Invention

The compounds of the present invention may be prepared by following the reaction sequences as depicted in the schemes in the accompanied drawings of which description is defined below

Mainly seventeen different amines of Formula VI identified as seventeen different cores, namely

(S)-N-[[3-[3-Fluoro-4-(N-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core I)

(S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-fluoroacetamide (Core II);

(S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-difluoroacetamide (Core III)

(S)-N-[[3-[3-Fluoro-4(N-1-piperazinyl)phenyl]]-2-oxo-5-oxazolidinyl]methyl] monochloro acetamide (Core IV)

(S)-N-[[3-[3-Fluoro-4 (N-1-piperazinyl)-phenyl]2-oxo-5-oxazolidinyl]methyl] –2-chloropropionamide (Core V)

(S)-N-[[3-[3[Fluoro-4-(N-1-homopiperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide (Core VI);

(S)-N-[[3-[3-Fluoro-4-{N-1-(2-methyl)piperazinyl}phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core VII);

(S)-N-[[3-[3-Fluoro-4-[N-1-{2,6-dimethyl-}-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]-methyl]acetamide (Core VIII);

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(S)-N-[[3-[3-Fluoro-4-[N-1-{3-methyl-}-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core IX);

(S)-N-[[3-[3-Fluoro-4-[{3-methyl-4-(N-methyl-)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core X);

(S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XI);

(S)-N-[[3-[3-Fluoro-4-(4-aminopiperidine-1-yl) phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XII);

(S)-N-[[3-[3-Fluoro-4-[4-{N-methyl-}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XIII);

(S)-N-[[3-[3-Fluoro-4[N-1, 3-[N-methyl aminopyrodinyl]phenyl]]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XIV);

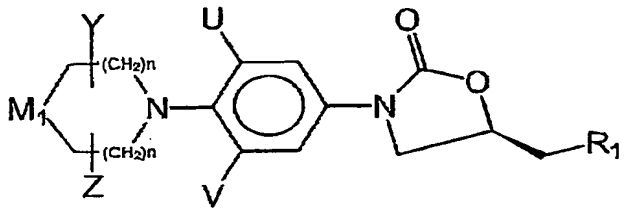
(S)-N-[[(3-[3-Fluoro-4-[N-1(4-N-methyl)-] aminomethyl piperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide (Core XV);

(S)-N[3-[3-[Fluoro-4-(N-1-(3-N-methyl)-aminopiperidinyl}-phenyl]2-oxo-5-oxazolidinyl]methyl]acetamide (Core XVI);

(S)-N-[[3-[3-Fluoro-4-{N-1-(N-aminomethyl)-3-azabicyclo[3.1.0]-hexane}phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XVII)

were used for analoguing purposes.

Key intermediate amines for the analogue preparation of compounds of Formula I are represented by Formula VI,



Formula VI

wherein

M_1 is NH, NHR_{13}, $-CH_2NHR_{13}$, $>C-CH_2NHR_{13}$, wherein R_{13} is H, ethyl, methyl, isopropyl, acetyl, cyclopropyl, alkoxy, or acetyl and n, R_1 U, V, Y and Z are as defined for Formula I.

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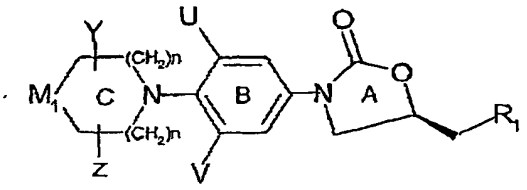
Some amines of Formula VI are already known in the literature and if they have been made for the first time or by a different procedure or variation of known procedure they are described in detail in the experimental section.

Optically pure amines of Formula VI could be obtained either by one of asymmetric syntheses methods known in the art or alternatively by resolution from a racemic mixture by selective crystallization of a salt prepared, with an appropriate optically active acid such as dibenzoyl tartrate or 10-camphorsulfonic acid, followed by treatment with base to afford the optically pure amine.

Scheme-I

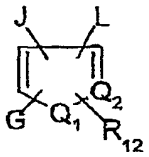
The compounds of the present invention represented by general Formula I may be prepared by the reaction sequence shown in Scheme I.

Scheme I

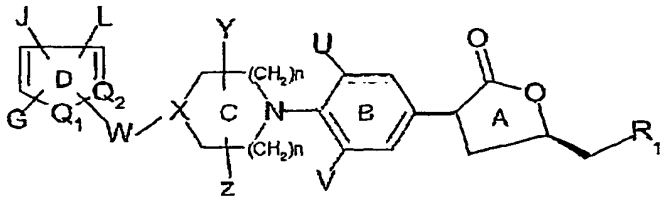


Formula VI

Method A
or
Method B
or
Method C



Formula VII



Formula I

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In Scheme I, the heteroaromatic group with the corresponding appendage can be introduced on the nitrogen atom of ring C of compounds of Formula VI by one of the methods described below to give the compounds of Formula I.

Amine of the structure of Formula VI wherein Y, Z, U, V, R_1 and n are the same as defined for Formula I and M_1 is the same as defined earlier, is reacted with a heteroaromatic compound of Formula VII wherein Q_1, Q_2, J, L and G are the same as defined for Formula I earlier; R_{12} is a suitable leaving group well known to one of ordinary skill in the art such as fluoro, chloro, bromo, SCH_3, -SO_2CH_3, -SO_2CF_3, Tosyl or OC_6H_5 etc

For the preparation of compounds of Formula I wherein W is equal to CH_2, corresponding aldehyde can be used through a process of reductive amination and is attached to amine of Formula VI.

Similarly, for the preparation of compound of Formula I wherein W is equal to C = O corresponding acid can be used and the amine of Formula VI can be acylated through activated esters in the presence of condensing agents such as 1,3-dicyclohexylcarbodiimide (DCC) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC). Other methods of acylation known in the art can also be employed.

Alternatively, the compounds of Formula I (W=CO) having carbonyl link can also be made by reacting heteroaromatic compound of the Formula VII such as N-methyl pyrrole with the intermediate amine of Formula VI in the presence of triphosgene or phosgene. Carbonyl linkers may also be introduced between heteroaromatic compound of Formula VII such as 3- bromothiophene and amine of Formula VI with carbon monoxide and the catalyst such as Pd $(PPh_3)_2Cl_2$. Extended chain pyrroles having dicarbonyl linkers can also be obtained from treatment with oxalyl chloride and amine of the Formula VI.

The reduction of the carbonyl linkers (W=CO) using the standard reducing agents results in the formation of methylene linkers ($W=CH_2$).

Preparation of the compound of Formula I is accomplished as exemplified below by three methods A, B and C as shown in Scheme I:

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Method A:

Amine of Formula VI is reacted with a heteroaromatic compound of Formula VII having R_{12} as a suitable leaving group defined earlier for Scheme I, R_1, Q_1, Q_2, G, J and L are the same as defined for Formula I.

The reaction is carried out in a suitable solvent such as dimethylformamide, dimethylacetamide, ethanol or ethylene glycol at a suitable temperature in the range of -70°C to 180°C to afford compounds of Formula I. The presence of a suitable base such as triethylamine, diisopropyl amine, potassium carbonate, sodium bicarbonate is useful in some cases to improve the yield of the reaction.

Method B:

Reductive alkylation of the amine intermediate of Formula VI, with the corresponding heterocyclic aldehydes of the Formula VII, such as furaldehyde (Q_1 = O, Q_2 = C; G, J, L = H; R_{12} is CHO) using known reducing agents well known to one of ordinary skill in the art such as sodium triacetoxyborohydride or sodium cyanoborohydride gave the products of Formula I wherein W=CH_2, as shown in the Scheme I.

Method C:

Acylation of intermediate amines of Formula VI with heterocyclic acid of Formula VII, such as 2- furoic acid (Q_1 = O; Q_2 = C; G, J, L = H; R_{12} =COOH) yield compound of Formula I, wherein W=CO, as shown in the Scheme I wherein U, V, Y, Z, X, W, Q_1, Q_2, G, J, L and are the are as defined earlier.

The reduction of the carbonyl linkers using the standard reducing agents results in the formation of methylene linkers.

SCHEME II

The compounds prepared by following the methods of Scheme I represented by Formula VIII (Formula I, when G=R_{14}) were further used as starting compounds for further derivatisation as shown in Scheme II

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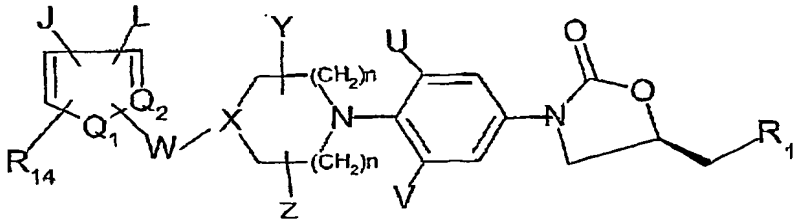
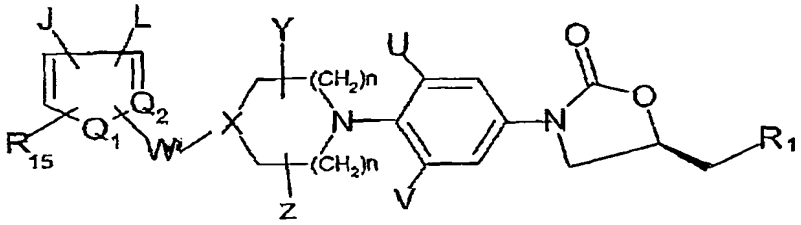
Scheme II



Formula VIII (Formula I, G = R_{14})

1 – 3 STEPS



Formula IX (Formula I, G = R_{15})

wherein R_1, U, V, Y, Z, X, W, Q_1, Q_2, J, L and n are the same as defined earlier. The group R_{14} (for example carbamate) is a subset of G in Formula I represented by Formula VIII, was transformed by carrying out one to three steps into final compounds of Formula IX, (Formula I when G=R_{15}).The transformed group R_{15}(for example amine, acetamide etc.), is also a subset of G group.

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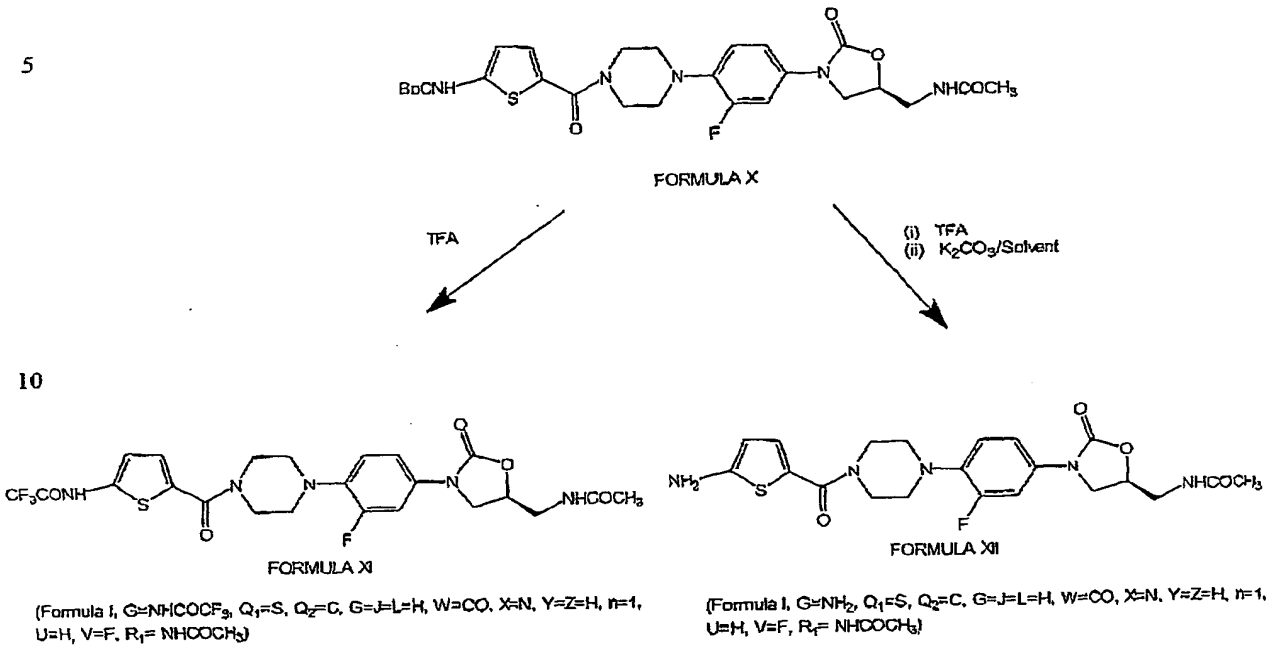
SCHEME IIA

The following compounds are exemplified in Scheme IIA

Scheme IIA



in which (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl(5-trifluoroacetamido)}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide represented by Formula XI (Formula I, G=$NHCOCF_3$, Q_1=S, O_2=C, G=J=L=H, W=CO, X=N, Y=Z=H, n=1, U=H, V=F, R_1=-$NHCOCH_3$) was prepared by treating the Boc derivative of Formula X with trifluoroacetic acid for extended time.

(S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl(5-amino)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide represented by Formula XII (Formula I G=NH_2, Q_1=S, O_2=C, G=J=L=H, W=CO, X=N, Y=Z=H, n=1, U=H, V=F, R_1=-$NHCOCH_3$) was prepared by treating the Boc derivative of Formula X with trifluoroacetic acid followed by neutralization with potassium carbonate in acetone as shown in Scheme IIA.

The transformations effected are described in the experimental section. In the above synthetic methods where specific acids, bases, solvents, catalysts,

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oxidising agents, reducing agents etc. are mentioned, it is to be understood that the other acids, bases, solvents, catalysts, oxidising agents, reducing agents etc. may be used. Similarly, the reaction temperature and duration of the reaction may be adjusted according to the need.

An illustrative list of particular compounds according to the invention and capable of being produced by the above mentioned schemes include:

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-(2-furyl-carbonylmethyl)]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 1),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-(2-thiophenoyl-methyl)]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 2),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl{5-(4-chloro-2-nitro-)-phenyl}methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide. (Compound No. 3),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen-(4-bromo-5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 4),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl-(3-methyl-5-nitro)methyl-}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 5),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-cyano-5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 6),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-(4-chloro)phenyl)methyl}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 7),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-furyl(5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 8),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-(4-bromo)phenyl)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 9),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-methyl)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide. (Compound No. 10),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-pyrrole-(1-methyl-4-nitro) methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide. (Compound No. 11),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-pyrrole-(1-methyl-5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 12),

BNSDOCID: <WO 03008389A1 I >

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-pyrrole-(5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl] acetamide. (Compound No. 13),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen-(4-nitro-)methyl-}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 14),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl-(5-methoxy)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 15),

- (S)-N-[[3-[3-Fluoro-4 [N-1 [4-[2-furyl {5-O-(2-nitro-4-fluoro-phenyloxy)} methyl]] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl] acetamide. (Compound No. 16),

- (S)-N-[[3-[3-Fluoro-4-[N-1[4-{2-furyl (5-chloro)methyl}] piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 17),

- (S)-N-[[3-[3-Fluoro-4-[N-1 [4-{3-furyl(2-nitro)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 18),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen-(4-dimethylamino-5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 19),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-morpholino-5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 20),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl-(5-methylsulphonyl-)methyl-}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 21),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-(4-nitro)-phenyl)-methyl}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 22),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-(3-nitro-)phenyl-)methyl}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 23),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-(2-nitro)-phenyl)-methyl}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 24),

- (S)-N-[[3-[3-Fluoro-4[N-1-[4-{2-Furyl-4-bromo-(5-nitro)methyl}]piperazinyl]-phenyl]-2-oxo-5-oxazolidinyl]methl]acetamide. (Compound No. 25),

- (S)-N-[[3-[3-Fluoro-4[N-1-[4-{2-Furyl-(4-isopropyl)methyl}]piperazinyl]-phenyl]-2-oxo-5-oxazolidinyl]methl]acetamide. (Compound No. 26),

- (S)-N-[[3-[3-Fluoro-4[N-1-[4-{2-Furyl-4-isopropyl(5-nitro)methyl}]piperazinyl]-phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide.(Compound No. 27),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl(5-methoxy)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 28),

BNSDOCID: <WO__03008389A1_I_>

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(5-acetamido)}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 29),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-pyrazolecarbonyl-(4-nitro)}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 30),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-pyrazolecarbonyl(5-nitro)}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 31),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(5-tert-butoxy-carboxamido)}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 32),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl(5-trifluoroacetamido)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 33),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl(5-amino)}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 34),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl{5-(4-chloro-2-nitro-)-phenyl}}] piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 35),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl-(3-methyl)}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 36),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl-(3-methyl-5-nitro)}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 37),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(4-dimethylamino-5-nitro)}] piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 38),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-Furoyl–(5-nitro)acrylic}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 39),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl–(5-nitro)acrylic}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 40),

- Iodide (S)-N-[[3-[3-Fluoro-4[N-1[4-N-methyl-4-{2-furyl(5-nitro)methyl}] piperazinyl]phenyl]-2-oxo-5-oxazolidinyl] methyl] acetamide. (Compound No. 41),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-nitro)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-fluoroacetamide. (Compound No. 42),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen(5-nitro)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]fluoroacetamide. (Compound No. 43),

BNSDOCID: <WO 03008389A1 I >

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen(5-nitro)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]difluoroacetamide (Compound No. 44),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-nitro)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-difluoroacetamide. (Compound No. 45),

- (S)-N-[[3-[3-Fluoro-4 [N-1 [4-{2-furyl (5-nitro)methyl}]piperazinyl]phenyl]]-2-oxo-5-oxazolidinyl]methyl]mono chloro acetamide. (Compound No. 46),

- (S)-N-[[3-[3-Fluoro-4[N-1[4-[2-thiophenyl-5-nitro)methyl}](Compound No. 47),

- (S)-N-[[3-[3-Fluoro-4 [N-1 [4-[2-thiophenyl-4bromo-(5-nitro)methyl}] piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl] monochloroacetamide. (Compound No. 48),

- (S)-N-[[3-[3-Fluoro-4 [N-1 [4-[2-thiophenyl--(5-nitro)methyl}]piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl]–2-chloropropionamide.(Compound No. 49),

- (S)-N-[[3-[3-Fluoro-4 [N-1 [4-[2-Furyl--(5-nitro)methyl}]piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl] –2-chloropropionamide. (Compound No. 50),

- (S)-N-[[3-[3-Fluoro-4 [N-1 [4-[2-thiophenyl-4-bromo-(5-nitro)methyl}] piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl]–2-chloropropionamide. (Compound No. 51),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-nitro) methyl}] homopiperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 52),

- (S)-N-[[3-[3-Fluoro-4-[N-1-{4-(3-furoyl)}homopiperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 53),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(5-nitro)}]homopiperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 54),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl(5-nitro)}]homopiperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No.55),

- (S)-N-[[3-[3-Fluoro-4-[N-1-{2-methyl-4-(t-butoxycarbonyl)}piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 56),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2-methyl-4-{2-thiophen-(5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 57),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2-methyl-4-{2-furyl(5-nitro)methyl}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 58),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2-methyl-4-{2-furoyl-(5-nitro)}]-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 59),

BNSDOCID: <WO__03008389A1_I_>

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2-methyl-4-{2-thiophenoyl-(5-nitro)}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 60),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furoyl-}]-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 61),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(5-formyl)methyl-}]-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Compound No. 62),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(5-nitro)methyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 63),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(5-hydroxymethyl)methyl-}]-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 64),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(aldoxime)methyl-}]-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 65),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-(2-thienylacetyl)]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 66),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(5-cyano)methyl-}]-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 67),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[3-methyl-4-{2-thienylacetyl-}]-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 68),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[3-methyl-4-{2-furoyl-(5-nitro)}]-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 69),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[3-methyl-4-{2-thienoyl-(5-nitro)}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 70),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-methyl-2-furyl-(5-formyl)methyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 71),
- (S)-N-[[3-[3-Fluoro-4-[4-{N-acetyl-N-2-furyl-(5-nitro)methyl-}]aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 72),
- (S)-N-[[3-[3-Fluoro-4-[{3-methyl-4-(N-methyl-N-thiophenacetyl-)}-amino piperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 73),
- (S)-N-[[3-[3-Fluoro-4-[[3-methyl-4-{N-methyl-2-furoyl(5-nitro)}]-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 74),

BNSDOCID: <WO 03008389A1 I >

- (S)-N-[[3-[3-Fluoro-4-[[3-methyl-4-{N-methyl-2-thienoyl-(5-nitro)}]-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (CompoundNo. 75),

- (S)-N-[[3-[3-Fluoro-4-[{3-methyl-4-(N-methyl-N-2-furoyl)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 76),

- (S)-N-[[3-[3-Fluoro-4-[[3-methyl-4-{N-methyl-N-2-furyl(5-nitro)}]-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 77),

- (S)-N-[[3-[3-Fluoro-4-[[3-methyl4-{N-methyl-N-2-thienyl-(5-nitro)}]-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 78),

- (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-2-thienoyl-(5-nitro)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 79),

- (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-2-furoyl-(5-nitro)}aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 80),

- (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-N-2-furoyl}-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 81),

- (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-N-2-thiophenacetyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 82),

- (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-N-2-thiophenyl-(5-nitro)methyl}-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 83),

- (S)-N-[[3-[3-Fluoro-4-[4-{N-thienyl-(5-nitro)methyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 84),

- (S)-N-[[3-[3-Fluoro-4-[4-{2-furyl-(5-nitro)methylene}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 85),

- (S)-N-[[3-[3-Fluoro-4-[4-{N-2-furyl-(5-nitro)methyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 86),

- (S)-N-[[3-[3-Fluoro-4-[4-{N-methyl-N-2-pyrrole-(5-nitro)methyl}-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 87),

- (S)-N-[[3-[3-Fluoro-4-[4-{N-methyl-N-2-furyl-(5-acetoxymethyl)methyl}-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 88),

- (S)-N-[[3-[3-Fluoro-4-[4-{N-methyl-N-2-furoyl-(5-nitro)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 89),

BNSDOCID: <WO__03008389A1_I_>

- (S)-N-[[3-[3-Fluoro-4[N-1,3-[N-methyl[N-{2-thiophenyl(5-nitro)methyl}] aminopyrodinyl]phenyl]]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 90),

- (S)-N-[[3-[3-Fluoro-4-[N-1,{3-{[N-methyl)[N-{2-thiophenoyl(5-nitro)}]amino pyrrolidinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 91),

- (S)-N-{[3-[3-Fluoro-4[N-1 [3-{(N-methyl)[N-2-furoyl(5-nitro)}]aminopryrolidinyl] phenyl]2-oxo-5-oxazolidinyl]methyl] acetamide. (Compound No. 92),

- (S)-N-[[(3-[3-Fluoro-4-[N-1[4-{N-methyl)-N-2-furyl-(5-nitro)-methyl}] aminomethylpiperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 93),

- (S)-N-[[3-[3-Fluoro-4[4-N-1(N-methyl){N-2-thiophenyl-(5-nitro)-methyl}] aminomethylpiperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 94),

- (S)-N-[[3-[3-Fluoro-4-{N-1[4-N-methyl)-N-2-furoyl(5-Nitro)-methyl}] aminomethylpiperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 95),

- (S)-N-[[3-{3-Fluoro-4-(3-oxo-piperidin-1-yl)-phenyl}-2-oxo-5-oxazolidinyl] methyl]acetamide. (Compound No. 96),

- (S)-N[3-{3-[Fluoro-4-[N-1-[3-N-methyl]-N-2-furyl (5-nitro)methyl}] aminopiperidinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl]acetamidezolidinyl] methyl]acetamide. (Compound No. 97),

- (S)-N-[[3-[3-Fluoro-4[N-1-[3-{2-furyl-(5-nitro)-methylene}aminomethyl]-3-azabiyclo(3.1.0)hexane]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 98),

- (S)-N-[[3-[3-Fluoro-4[N-1[3-{N-2-furyl-(5-nitro)methyl}-aminomethyl]-3-azabicyclo[3.1.0]hexane]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 99),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-[1-{2-thiophenyl-(5-nitro)}-1-ethyl]]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 100),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-[1-{2-furyl-(5-nitro)}-1-ethyl]]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 101),

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-(4-t-butoxycarbonyl)piperazinyl-5-nitro)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 102),

BNSDOCID: <WO 03008389A1 I >

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-N-piperazinyl-5-nitro)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 103),
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-(4-methyl)piperazinyl-5-nitro)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 104),

Pharmacological Testing

The compounds of the invention display antibacterial activity when tested by the agar incorporation method. The following minimum inhibitory concentrations (µg/ml) were obtained for representative compounds of the invention which are given below in the following tables.

GUIDE TO TABLE ABBREVIATIONS:

1) *S.aureus* ATCC 25923 –*Staphylococus aureus* ATCC 25923

2) MRSA 15187 –Methicillin Resistant *Staphylococcus aureus*

3) *Ent. faecalis* ATCC 29212 –*Enterococcus faecalis* ATCC 29212

4) *Ent. faecium* 6A – *Enterococcus faecium 6A Van®,Cipro®*

5) *Strep. pne.* ATCC 6303 –*Streptococcus pneumoniae* ATCC 6303

6) *Strep.pyog.* ATCC 19615 –*Streptococcus pyogenes*

7) *S. epidermidis* - *Staphylococcus epidermidis* ATCC 12228

In vitro (MIC) (µg/ml)

Compound No.	*S.aureus* 25923	MRSA 15187	MRSA 562	MRSA 33	E.faecalis 29212	VRE 6A	*S.pyogenes 19615*	*S. pneum 6303*	*S. pneum* AB 34
2	8	8	4	4	8	8	2	2	8
4	2	1	1	2	2	2	4	4	4
5	2	2	2	0.254	2	4	0.5	1	1
6	2	2	2	2	4	8	1	1	1
8	8	8	4	4	8	4	4	8	16
11	4	4	4	4	4	4	2	2	4
12	4	4	4	4	4	4	2	8	8
13	4	2	4	4	4	4	1	4	4
14	0.25	0.25	0.25	0.25	4	2	0.5	2	1
15	4	4	4	4	4	4	2	2	2
18	8	4	4	4	4	4	1	1	2

BNSDOCID: <WO__03008389A1 I_>

Compound No.	*S.aureus* 25923	MRSA 15187	MRSA 562	MRSA 33	E.faecalis 29212	VRE 6A	*S.pyogenes 19615*	*S. pneum 6303*	*S. pneum* AB 34
19	4	4	8	8	4	4	2	2	2
25	2	1	2	2	2	2	0.5	2	2
29	8	4	4	4	4	4	0.5	0.5	1
31	>8	>8	>8	>8	4	4	1	1	1
34	8	8	4	8	4	4	1	4	4
35	1	1	1	1	0.5	1	1	1	1
36	2	2	2	2	2	1	1	0.5	1
37	0.5	0.5	0.5	0.5	0.25	0.5	<0.06	0.25	0.125
38	8	4	4	4	4	4	2	2	2
39	0.5	0.5	0.25	0.25	0.5	<0.125	<0.125	0.5	4
40	0.5	0.25	1	0.5	1	0.5	0.5	1	1
42	4	2	2	4	4	4	0.5	1	2
45	2	1	2	2	2	2	0.5	0.5	2
46	2	2	2	2	2	2	0.5	0.5	1
47	4	4	4	4	4	4	1	2	4
48	4	4	4	4	2	2	16	16	16
51	8	8	8	8	8	8	16	16	16
52	2	2	1	2	2	2	1	1	4
54	1	0.5	0.5	0.5	1	0.5	0.25	8	8
55	2	0.5	1	2	0.25	0.25	4	8	8
58	4	4	2	4	4	4	4	8	16
59	2	1	1	1	1	2	8	8	8
60	0.25	<0.125	<0.125	<0.125	1	1	0.5	4	4
61	4	4	4	4	4	4	2	2	2
63	16	8	8	8	8	8	16	16	16
66	8	8	8	8	8	8	16	16	16
68	4	4	4	4	4	4	2	4	4
69	1	1	0.5	1	0.5	0.5	2	8	8
70	<0.25	0.5	<0.25	<0.25	2	1	<0.25	4	4
71	4	2	2	4	>8	>8	>8	>8	>8
74	<0.5	<0.5	<0.5	1	1	1	8	8	8
79	0.5	0.5	0.5	0.5	2	2	0.5	4	4
80	1	1	0.5	1	1	1	2	4	4
83	4	4	4	4	4	4	8	8	8
84	2	2	2	2	1	2	1	2	2
85	4	4	4	4	>8	>8	2	4	4
86	1	1	1	1	0.5	0.5	<0.25	2	2
90	4	2	2	4	4	4	2	4	4
93	2	1	1	1	2	4	1	4	4
91	<0.25	<0.25	<0.25	<0.25	0.5	1	<0.25	1	1
92	1	0.5	<0.25	0.5	<0.25	<0.25	1	1	1
94	4	2	2	2	4	4	4	4	8
95	1	1	0.5	1	<0.25	0.5	–	--	–
96	16	16	8	16	8	8	4	4	4
99	>8	>8	>8	>8	>8	8	2	4	4
100	0.5	0.5	0.5	0.5	0.5	0.5	2	2	2
101	1	1	1	1	0.125	0.25	0.06	1	2

The *in vitro* antibacterial activity of the compounds were demonstrated by the agar incorporation method (NCCLS M 7 and M 100-S8 documents). Briefly, the compounds were dissolved in DMSO and doubling dilution of the compounds were incorporated into Mueller Hinton agar before solidification. Inoculum was

BNSDOCID: <WO 03008389A1 | >

prepared by suspending 4 to 5 colonies into 5 ml of normal saline solution and adjusting the turbidity to 0.5 Macfarland turbidity standard tables (1.5×10^8 CFU/ml), after appropriate dilutions, 10^4 CFU/spot was transfered into the surface of dried plate and incubated for 18 hours (24 hours for MRSN studies). The concentration showing no growth of the inoculated culture was recorded as the MIC. Appropriate ATCC standard strains were simultaneously tested and result recorded only when the MIC's against standard antibiotics were within the acceptable range.

The compounds of the present invention represented by general Formula I may be prepared by the method of reaction in Scheme I. Key intermediate amines of Formula VI for the analogue preparation were prepared by the synthetic procedures described below, from commercially available reagents. The compounds of Formula I were made by either Method A, B, or C.

Amines already known in the literature are given by reference and if they have been made by a different procedure they are described in detail.

Mainly following seventeen different amines of Formula VI were identified as different cores, namely

(S)-N-[[3-[3-Fluoro-4-(N-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core I);

(S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-fluoroacetamide (Core II);

(S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-difluoroacetamide (Core III),

(S)-N-[[3-[3-Fluoro-4--(N-1-piperazinyl)phenyl]]-2-oxo-5-oxazolidinyl]methyl] monochloroacetamide (Core IV),

(S)-N-[[3-[3-Fluoro-4 (N-1-piperazinyl)-phenyl]2-oxo-5-oxazolidinyl]methyl]--2-chloropropionamide (Core V),

(S)-N-[[3-[3[Fluoro-4-(N-1-homopiperazinyl)phenyl]-2-oxo-5-oxazolidinyl]-methyl] acetamide (core VI),

(S)-N-[[3-[3-Fluoro-4-{N-1-(2-methyl)piperazinyl}phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core VII),

BNSDOCID: <WO__03008389A1_I_>

(S)-N-[[3-[3-Fluoro-4-[N-1-{2,6-dimethyl-}-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]-methyl]acetamide (Core VIII),

(S)-N-[[3-[3-Fluoro-4-[N-1-{3-methyl-}-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core IX),

(S)-N-[[3-[3-Fluoro-4-[{3-methyl-4-(N-methyl-)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core X),

(S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XI),

(S)-N-[[3-[3-Fluoro-4-(4-aminopiperidine-1-yl) phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XII),

(S)-N-[[3-[3-Fluoro-4-[4-{N-methyl-}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XIII),

(S)-N-[[3-[3-Fluoro-4[N-1, 3-[N-methyl aminopyrodinyl]phenyl]]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XIV),

(S)-N-[[(3-[3-Fluoro-4-[N-1(4-N-methyl)-] aminomethyl piperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide (Core XV),

(S)-N[3-[3-[Fluoro-4-{N-1-(3-N-methyl)-aminopiperidinyl}-phenyl]2-oxo-5-oxazolidinyl]methyl]acetamide (Core XVI),

(S)-N-[[3-[3-Fluoro-4-{N-1-(N-aminomethyl)-3-azabicyclo[3.1.0]-hexane}phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XVII)

The mentioned cores were used for the synthesis of compounds of this invention.

Most of the compounds were characterized using NMR, IR and were purified by chromatography. Crude products were subjected to column chromatographic purification using silica gel (100-200 or 60-120 mesh) as stationary phase.

The examples mentioned below demonstrate the general synthetic procedure as well as the specific method for the preparation of the preferred compound. The examples are given to illustrate the details of the invention and should not be constrained to limit the scope of the present invention.

BNSDOCID: <WO 03008389A1 I >

EXAMPLE 1

Analogues of (S)-N-[[3-[3-Fluoro-4-(N-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide(core I)

The heteroaromatic group with the corresponding appendage can be introduced on the nitrogen atom of ring C of compounds of Formula I by one of the methods described below:

Method A:

General procedure:

Amine of structure of Formula VI is reacted with a heteroaromatic compounds of Formula VII having corresponding R_{12} appendages such as - CH_2R_{13}, -COR_{13} or - $CH(CH_3)R_{13}$ wherein R_{13} is a suitable leaving group well known to one of ordinary skill in the art such as fluoro, chloro, bromo, SCH_3, - SO_2CH_3, -SO_2CF_3, Tos or OC_6H_5 etc.

The reaction is done in a suitable solvent such as dimethylformamide, dimethylacetamide, ethanol or ethylene glycol at a suitable temperature in the range of -78°C to 180°C to afford compounds of Formula II. The presence of a suitable base such as triethylamine, diisopropyl amine, potassium carbonate, sodium bicarbonate is useful in some cases to improve the yield of the reaction.

The following compounds were made using this method:

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-(2-furyl-carbonylmethyl)] piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 1)

To the mixture of (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl-]-acetamide (prepared by following the method described in US patent No. 5,700,799; 0.57 mmol) and 2-chloroacetylfuran (0.13 g, 0.86 mmol) (prepared by following the method described in J. Am. Chem. Soc., 57, 909-912, 1935) in dimethyl formamide (10 mL), potassium carbonate (0.24 g, 1.72 mmol) was added and stirred for 1 hr. The reaction mixture was then diluted with water and extracted with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulphate and evaporated in vacuo. The crude product was

BNSDOCID: <WO 03008389A1 I >

purified by column chromatography (MeOH/$CHCl_3$) to get the title compound (0.1 g).

^{1}HNMR ($CDCl_3$) δppm : 7.62 (s, 1H), 7.5 (d, 1H), 7.38 (s, 1H), 7.06 (m, 1H), 6.96 (t, 1H), 6.57 (s, 1H), 6.01 (m, 1H), 4.77 (m, 1H), 4.03 (t, 1H), 3.85-3.5 (m, 5H), 3.2 (m, 4H), 2.89 (m, 4H), 2.03 (s, 3H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-(2-thiophenoyl-methyl)]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 2)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 2-chloroacetylthiophene using Method A

^{1}HNMR ($CDCl_3$) δppm : 7.94 (d, 1H), 7.63 (d, 1H), 7.39 (d, 1H), 7.12 (m, 1H), 7.05 (m, 1H), 6.93 (t, 1H), 6.08 (m, 1H), 4.75 (m, 1H), 4.01 (t, 1H), 3.8-3.4 (m, 5H), 3.14 (m, 4H), 2.79 (m, 4H), 2.01 (s, 3H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl{5-(4-chloro-2-nitro-)-phenyl}methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide. (Compound No. 3)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-(4-chloro-2-nitro)-phenyl-2-chloromethyl-furan using Method A

^{1}HNMR ($CDCl_3$) δppm: 7.68 (m, 2H), 7.55 (d, 1H), 7.44 (d, 1H), 7.02 (m, 1H), 6.92 (t, 1H), 6.62 (d, 1H), 6.38 (d, 1H), 6.07 (t, 1H), 4.77 (m, 1H), 4.01 (t, 1H), 3.9-3.7 (m, 5H), 3.10 (m, 4H), 2.71 (m, 4H), 2.01 (s, 3H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen-(4-bromo-5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 4)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 4-bromo-5-nitro-2-

BNSDOCID: <WO 03008389A1_I_>

chloromethylthiophene (prepared by following the method described in J. Med. Chem. 2000, 43, 2258-2265) using Method A.

^{1}HNMR ($CDCl_3$) δppm: 7.47 (m, 1H), 7.1-6.6 (m, 3H), 6.05 (m, 1H), 4.77 (m, 1H), 4.1-2.5 (m, 4H), 2.03 (s, 3H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl-(3-methyl-5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 5)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 3-methyl-5-nitro-2-chloromethylfuran using Method A.

^{1}HNMR ($CDCl_3$) δppm: 7.46 (dd, 1H), 7.18 (s, 1H), 7.04 (dd, 1H), 6.93 (t, 1H), 6.05 (m, 1H), 4.77 (m, 1H), 4.1-3.5 (m, 6H), 3.22 (m, 4H), 2.91 (m, 4H), 2.21 (s, 3H), 2.02 (s, 3H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-cyano-5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 6)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 4-cyano-5-nitro-2-chloromethylthiophene using Method A.

^{1}HNMR ($CDCl_3$) δppm: 7.44 (m, 1H), 7.2-6.7 (m, 3H), 6.04 (m, 1H), 4.76 (m, 1H), 4.1-2.6 (m, 14H), 2.02 (s, 3H)

M+1 = 503

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-[1-{2-thiophenyl-(5-nitro)}-1-ethyl]]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 100)

To a mixture of (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide (0.65 g, 1.93 mmol) in tetrahydrofuran (20 mL),

BNSDOCID: <WO__03008389A1_I_>

triethylamine (0.8 mL, 5.8 mmol) was added and the resultant mixture cooled to 0° C. 5-nitro-2-(α-methylsulfonate)ethylthiophene (0.885 g, 2.9 mmol) dissolved in tetrahydrofuran (10 mL) was added and the reaction mixture stirred at room temperature for 24 hrs. It was then diluted with ethylacetate and washed with saturated sodium bicarbonate solution, water and brine solution. The organic layer was dried over anhydrous sodium sulphate and evaporated in *vacuo*. The residue was purified by silica gel column chromatography using dichloromethane-methanol as eluents (Yield=0.612 g).

^{1}HNMR ($CDCl_3$) δppm: 2.02 (s, 3H), 2.69-2.72 (m, 6H), 3.01-3.06 (q, 2H), 3.12-3.14 (br s, 4H), 3.63-3.77 (m, 3H), 4.0-4.06 (q, 1H), 4.76 (br s, 1H), 6.13 (s, 1H), 6.8-6.81 (d, 1H), 6.93-6.96 (t, 1H), 7.04-7.07 (t, 1H), 7.42-7.46 (dd, 1H), 7.76-7.78 (d, 1H)

Preparation of 5-nitro-2-(α-Trifluoromethylsulfonate)ethylthiophene

(a) 5-nitro-2-(α-hydroxy)ethylthiophene: 5-nitro-2-acetylthiophene (0.85 g, 4.97 mmol; Synthesis, 1992, 849-851) was taken in 25 ml of tetrahydrofuran and cooled to 0° C . Sodium borohydride (0.19 g, 4.97 mmol) was added to the above, followed by 25 ml of water. The reaction mixture was allowed to come to room temperature and stirring was further continued for about 3 hrs. The reaction mixture was then diluted with ethyl acetate and washed with water and brine solution. The combined organic layers were dried over anhydrous sodium sulphate and then concentrated *in vacuo* (Yield=652 mg).

^{1}HNMR ($CDCl_3$) ppm: 1.60-1.66 (d, 3H), 2.41 (br s, 1H), 5.11-5.13 (d, 1H), 6.88- 6.9 (d, 1H), 7.79-7.81 (d, 1H).

(b)5-nitro-2-(α-Trifluoromethylsulfonate)ethylthiophene:5-nitro-2-(α-hydroxy)ethylthiophene (650 mg, 3.76 mmol) was taken in 10 ml of dichloromethane and cooled to 0°C. Triflic anhydride (0.95 ml, 5.64 mmol) was added at 0° C and the reaction mixture was allowed to come to room temperature and stirring was further continued for about 3 hrs. The reaction mixture further diluted with dichloromethane and washed with sodium bicarbonate solution, water and brine solution. The combined organic layers were dried over anhydrous

BNSDOCID: <WO 03008389A1 I >

sodium sulphate and then concentrated *in vacuo*. The crude product obtained was used for the next reaction without further purification (Yield=940 mg).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-[1-{2-furyl-(5-nitro)}-1-ethyl]]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 101)

To a mixture of (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide (0.25 g, 0.744 mmol) in tetrahydrofuran (20 mL), triethylamine (0.3 mL, 2.23214 mmol) was added and the resultant mixture was cooled to 0° C. To it, **5-nitro-2-(α-Trifluromethylsulfonate)ethylfuran** (0.43 g, 1049 mmol) dissolved in tetrahydrofuran (10 mL) was added and the reaction mixture stirred at room temperature for 24 hrs. It was then diluted with ethyl acetate and washed with saturated sodium bicarbonate solution, water and brine solution. The organic layer was dried over sodium sulphate and evaporated in vacuo. The residue was purified by silica gel column chromatography using dichloromethane-methanol as eluents (Yield 0.2 g, m.p.: 144-46°C).

^{1}HNMR ($CDCl_3$) δppm: 2.015 (s, 3H), 2.68-2.7 (d, 4H), 2.80-2.82 (m, 2H), 2.84-2.89 (t, 2H), 3.07-3.1 (s, 4H), 3.46-3.7 (m, 3H), 4.01 (t, 1H), 4.7 (br s, 1H), 5.29 (s, 1H), 6.05 (br s, 1H), 6.37 (s, 1H), 6.89-6.91 (t, 1H), 7.04-7.07 (d, 1H), 7.4-7.45 (d, 1H).

Preparation of 5-nitro-2-(α-Trifluoromethylsulfonate)ethylfuran

(a) **5-nitro-2-acetylfuran:** 58 ml of acetic anhydride was cooled to –30° C and 23.1 ml of fuming HNO_3 was added to acetic anhydride dropwise at –30° C. In another flask, 10g of 2-acetyl furan was dissolved in 21.6 ml of acetic anhydride and added to the nitration mixture at –30°C dropwise. The reaction mixture was stirred at –30° to –0° C for about 4 hours and then was poured over ice and neutralized with 40% NaOH solution (up to pH –6). The reaction mixture was then extracted the with ethyl acetate (3x100ml). To the ethyl acetate layer 10 ml of pyridine was added and further kept for 1 hour. This mixture was then washed

BNSDOCID: <WO__03008389A1_I_>

with saturated citric acid solution, water and brine solution. The combined organic layers were dried over anhydrous sodium sulphate and evaporated *in vacuo*. The residue was purified by silica gel column chromatography using hexane-ethyl acetate mixture as eluent (Yield: 625 mg).

^{1}HNMR ($CDCl_3$) δppm: 2.39 (s, 3H), 7.26-d 7.28 (s, 1H), 7.36-7.38 (s, 1H)

(b) **5-nitro-2-(α-hydroxy)ethylfuran**: 5-nitro-2-acetylfuran (1g, 6.45 mmol) was taken in 25 ml of tetrahydrofuran and cooled to 0°C. Sodium borohydride was added to the above, followed by 25 ml of water. The reaction mixture was allowed to come to room temperature and stirring was further continued for about 3 hrs. The reaction mixture was then diluted with ethyl acetate and washed with water and brine solution. The combined organic layers were dried over anhydrous sodium sulphate and then concentrated *in vacuo*. The crude product obtained was used for the next reaction without further purification (Yield = 625mg).

^{1}HNMR ($CDCl_3$) δppm: 1.60 (d, 3H), 4.99 (q, 1H), 6.50- 6.51 (d, 1H), 7.27-7.28 (d, 1H).

(c) **5-nitro-2-(α-trifluoromethylsulfonate)ethylfuran**: To a mixture of 5-nitro-2-(α-hydroxy)ethylfuran (400 mg, 2.5477 m.moles) and dichloromethane (10 ml), triethylamine (0.7 m, 5.0955 m.moles) was added and the reaction mixture cooled to 0° C. Triflic anhydride (0.6 ml, 3.8216 m.moles) was added at 0° C and then the reaction mixture was allowed to stir at room temperature for another 6 hours. The reaction mixture was further diluted with dichloromethane and washed with sodium bicarbonate solution, water and brine solution dried. The combined organic layers were dried over sodium sulphate and evaporated *in vacuo*. The crude product obtained was used for the next reaction without further purification (Yield=410 mg).

BNSDOCID: <WO 03008389A1 I >

Method B

General Procedure:

Reductive alkylation of the amine intermediate of Formula VI, with the corresponding heterocyclic aldehydes of the Formula VII, using known reducing agents well known to one of ordinary skill in the art such as sodium triacetoxyborohydride or sodium cyanoborohydride gave the products of Formula I wherein W=CH_2.

The following compounds were made using this method:

Prepararion of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-[2-furyl(5-(4-chloro)phenyl) methyl}]-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 7)

To a mixture of (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide (1.14 mmol) and 5-(4-chloro)phenyl-2-furfuraldehyde (1.37 mmol) in tetrahydrofuran, freshly activated molecular sieves were added and stirred for 45 min. Then, sodium triacetoxyborohydride (0.29 g, 1.37 mmol) was added and stirred for 1-17 hrs. It was then filtered and filterate evaporated in vacuo. The crude product was purified by column chromatography (1%, 2% MeOH/ $CHCl_3$) to get the title compound (0.126 g)

^{1}HNMR ($CDCl_3$) δppm: 7.7-7.3 (m, 5H), 7.04 (m, 1H), 6.92 (t, 1H), 6.58 (d, 1H), 6.32 (d, 1H), 5.95 (m, 1H), 4.74 (m, 1H), 4.01 (t, 1H), 3.8-3.5 (m, 5H), 3.11 (m, 4H), 2.74 (m, 4H), 2.01 (s, 3H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-[3-furyl(5-nitro)methyl}] piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No.8)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-3-furfuraldehyde (prepared by following method described in J. Am. Chem. Soc. , 1933, 55, 2903-2909) using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.6-7.3 (m, 3H), 7.07 (m, 1H), 6.92 (t, 1H), 6.06 (m, 1H), 4.76 (m, 1H), 4.41 (m, 1H), 4.0 (m, 2H), 3.8-2.8 (m, 9H), 2.65 (m, 2H), 2.01 (s, 3H).

BNSDOCID: <WO_03008389A1 I >

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-(4-bromo)phenyl) methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 9)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-(4-bromo)phenyl-2-furfuraldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.6-7.3 (m, 5H), 7.06 (m, 1H), 6.92 (t, 1H), 6.60 (d, 1H), 6.4 (d, 1H), 6.00 (m, 1H), 4.75 (m, 1H), 4.0 (t, 1H), 3.8-3.5 (m, 5H), 3.2-2.6 (m, 8H), 2.0 (s, 3H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-methyl)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide. (Compound No. 10)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-methyl-2-furfuraldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.39 (dd, 1H), 7.03 (m, 1H), 6.92 (t, 1H), 6.11 (d, 1H), 6.02 (m, 1H), 5.9 (d, 1H), 4.76 (m, 1H), 4.00 (t, 1H), 3.8-3.4 (m, 5H), 3.11 (m, 4H), 2.67 (m, 4H) 2.28 (s, 3H), 2.01 (s, 3H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-pyrrole-(1-methyl-4-nitro) methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide. (Compound No. 11)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 1-methyl-4-nitro-pyrrole-2-aldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.46 (s, 1H), 7.4 (dd, 1H), 7.05 (m, 1H), 6.89 (t, 1H), 6.6 (s, 1H), 6.24 (t, 1H), 4.75 (m, 1H), 4.0 (t, 1H), 3.8-3.5 (m, 6H), 3.45 (s, 2H), 3.02 (m, 4H), 2.59 (m, 4H), 2.01 (s, 3H)

BNSDOCID: <WO 03008389A1 I >

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-pyrrole-(1-methyl-5-nitro) methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 12)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 1-methyl-5-nitro-pyrrole-2-aldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.42 (dd, 1H), 7.16 (d, 1H), 7.05(m, 1H), 6.9 (t, 1H), 6.1 (d, 1H), 5.97 (m, 1H), 4.75 (m, 1H), 4.04 (m, 4H), 3.8-3.4 (m, 5H), 3.04 (m, 4H), 2.6 (m, 4H), 2.01 (s, 3H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-pyrrole-(5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl] acetamide. (Compound No. 13)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-pyrrole-2-aldehyde (Bull. Soc. Chim. France, 1963, 484-487) using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.42 (dd, 1H), 7.06 (m, 2H), 6.91 (t, 1H), 6.37 (m, 1H), 6.16 (d, 1H), 4.77 (m, 1H), 4.01 (t, 1H), 3.76 (t, 1H), 3.65 (m, 5H), 3.08 (m, 4H), 2.68 (m, 4H), 2.02 (s, 3H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen-(4-nitro-)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 14)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 4-nitro-2-thiophenaldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 8.24 (s, 1H), 7.53 (s, 1H), 7.44 (dd, 1H), 7.06 (d, 1H), 6.93 (t, 1H), 6.14 (t, 1H), 4.76 (m, 1H), 4.2-3.4 (m, 6H), 3.14 (m, 4H), 2.75 (m, 4H), 1.93 (s, 3H)

BNSDOCID: <WO__03008389A1_I_>

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl-(5-methoxy)methyl}] piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 15)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-methoxy-2-furaldehyde (Khim. Geterosikl. Soedin, 1982, (6), 747-50) using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.43 (dd, 1H), 7.03 (m, 1H), 6.91 (t, 1H), 6.1 (m, 2H), 5.06 (d, 1H), 4.8 (m, 1H), 3.97 (t, 1H), 3.8-3.4 (m, 8H), 3.08 (m, 4H), 2.66 (m, 4H), 2.01 (s, 3H)

Preparation of (S)-N-[[3-[3-Fluoro-4 [N-1 [4-[2-furyl {5-O-(2-nitro-4-fluoro-phenyloxy)}methyl]]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide. (Compound No. 16)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4[N-1-piperazinylphenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-O-(2-nitro-4-fluoro)-phenyloxy-2-furaldehyde (Chem. Pharm. Bull. 28(9), 2846-2849, 1980) using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.8 (d, 1H, Ar-H), 7.7 (d, 1H, Ar-H), 7.1-7.4 (m, 4H, Ar-H), 6.2 (d, 1H, Ar H), 6.0 (t, 1H, NH) 5.6 (d, 1H, Ar-H), 4.7 (m, 1H, CH), 4.0 (t, 1H, CH), 3.4-3.6 (m, 5H, CH_2), 3.1 (m, 4H, CH_2), 2.6 (m, 4H, CH_2), 2.0 (s, 3H, CH_3)

IR : 1748, 1654cm^{-1}

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1[4-{2-furyl (5-chloro)methyl}] piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 17)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[N-1-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-chloro-2-furaldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.8 (d, 1H, Ar-H), 7.6 (m, 1H, Ar-H), 7.4 (m, 1H, Ar-H), 6.4 (m, 1H, Ar-H), 6.0 (m, 1H, Ar-H), 4.7 (m, 1H, CH), 4.0 (m, 2H, CH_2), 3.8 (m, 4H, CH_2), 3.6 (m, 4H, CH_2), 3.4 (m, 4H, CH_2), 2.0 (s, 3H, CH_3)

BNSDOCID: <WO 03008389A1 I >

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1 [4-{3-furyl(2-nitro)methyl}] piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 18)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[N-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 2-nitro-3-furaldehyde (J.Org. Chem.1989,54,5094-5100) using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.3-7.5 (m, 2H, Ar-H), 7.1 (d, 1H, Ar-H), 6.9 (t, 1H, Ar-H), 6.8 (d, 1H, Ar-H), 6.0 (t, 1H, NH), 4.7 (m, 1H,CH), 4.0 (t, 1H, CH), 3.9 (s, 2H, CH_2), 3.6-3.8 (m, 3H, CH_2), 3.1 (m, 4H, CH_2), 2.8 (m,4H, CH_2), 2.0 (s, 3H, CH_3)

IR: 1743, 1654 cm^{-1}

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen-(4-dimethylamino-5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 19)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[N-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 4-dimethylamino-5-nitro-2-thiophenaldehyde (J. Med. Chem., 2000, 43, 2258-65) using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.44 (dd, 1H), 7.06 (m, 1H), 6.93 (t, 1H), 6.56 (s, 1H), 6.15 (t, 1H), 4.76 (m, 1H), 4.02 (t, 1H), 3.5-3.9 (m, 5H), 3.11 (m, 10H), 2.71 (m, 4H), 2.02 (s, 3H).

M+1 =521; m.p= 135 °C

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-morpholino-5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 20)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[N-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 4-morpholino-5-nitro-2-thiophenaldehyde (prepared by following the method as described in J. Med. Chem., 2000, 43, 2258-65, wherein instead of dimethylamine hydrochloride, morpholine was used) using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.44 (m, 1H), 7.06 (m, 1H), 6.93 (t, 1H), 6.60 (s, 1H), 6.09 (t, 1H), 4.75 (m, 1H), 3.5-4.1 (m, 10H), 3.39 (m, 4H), 3.11 (m, 4H), 2.73 (m, 4H), 2.02 (s, 3H)

BNSDOCID: <WO_03008389A1_I_>

M+1 = 563; m.p. = 188-191 °C

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl-(5-methylsulphonyl-)methyl-}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 21)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[N-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-methylsulphonyl-2-furaldehyde (prepared by following the method as described in Chem. Abs. 71:101697d) using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.42 (m, 1H), 7.13 (d, 1H), 7.05 (m,1H), 6.94 (t, 1H), 6.42 (d, 1H), 6.09 (m,1H), 4.76 (m, 1H), 4.01 (t, 1H), 3.3-3.8 (m, 5H), 3.17 (s, 3H), 3.09 (m, 4H), 2.7 (m, 4H), 2.04 (s, 3H)

M+1=495

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-(4-nitro)-phenyl)-methyl}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 22)

The title compound was prepared with (S)-N-[[3-[3-Fluoro-4-[N-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-(4-nitro)phenyl-2-furaldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 8.23 (d, 2H), 7.79 (d, 2H), 7.42 (dd, 1H), 7.06 (m, 1H), 6.92 (t, 1H), 6.83 (d, 1H), 6.41 (d, 1H), 6.06 (t, 1H), 4.74 (m, 1H), 3.97 (t, 1H), 3.4-3.8 (m, 5H), 3.12 (m, 4H), 2.75 (m, 4H), 2.08 (s, 3H)

M+1 = 538

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-(3-nitro-)phenyl-)methyl}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 23)

BNSDOCID: <WO 03008389A1 I >

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[N-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-(3-nitro)phenyl-2-furaldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 8.49 (s, 1H), 8.08 (d, 1H), 7.96 (d, 1H), 7.54 (t, 1H), 7.42 (dd, 1H), 7.04 (m, 1H), 6.94 (m, 1H), 6.76 (d, 1H), 6.39 (d, 1H), 6.02 (t, 1H), 4.75 (m, 1H), 4.01 (t, 1H), 3.9-3.4 (m, 5H), 3.12 (m, 4H), 2.74 (m,1H), 2.01 (s, 3H)

M+1 = 538

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl-(5-(2-nitro)-phenyl)-methyl}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 24)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[N-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-(2-nitro)phenyl-2-furaldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.7 (m, 2H), 7.58 (t, 1H), 7.41 (m, 2H), 7.03 (m, 1H), 6.94 (t, 1H), 6.61 (d, 1H), 6.36 (d, 1H), 5.99 (t, 1H), 4.75 (m, 1H), 4.00 (t, 1H), 3.8-3.25 (m, 5H), 3.11 (m, 4H), 2.71 (m, 4H), 2.01 (s, 3H)

M+1= 538

Preparation of (S)-N-[[3-[3-Fluoro-4[N-1-[4-{2-Furyl-4-bromo-(5-nitro) methyl}] piperazinyl]-phenyl]-2-oxo-5-oxazolidinyl]methl]acetamide. (Compound No. 25)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[N-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 4-bromo-5nitro-2-furaldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.45(d,1H,Ar-H),7.1(d,1H,Ar-H).6.9(m,1H,Ar-H),6.65(s,1H,Ar-H),6.0(m,1H,NH),4.78(m,1H,CH),4.0(m,1H,CH),3.8-3.6(m,5H,CH_2), 3.1(m,4H,CH_2), 2.8(m,4H,CH_2)2.0(s,3H,CH_3).

BNSDOCID: <WO_03008389A1_I_>

Preparation of (S)-N-[[3-[3-Fluoro-4[N-1-[4-{2-Furyl-(4-isopropyl)methyl}] piperazinyl]-phenyl]-2-oxo-5-oxazolidinyl]methl]acetamide. (Compound No. 26)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[N-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 4-Isopropyl-2-furaldehyde(J.Org Chem.,1976 ,41,2835-2846) using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.4(d,1H,Ar-H),7.2(d,1H,Ar-H),7.0(m,1H,Ar-H),6.9(m,1H,Ar-H),6.2(m,2H,Ar-H,andNH),4.77(m,1H,CH),4.0(m,1H,CH),3.8-3.6(m,6HCH_2)2.8(m,4H,CH_2), 2.0(s,3H,CH_3

Preparation of (S)-N-[[3-[3-Fluoro-4[N-1-[4-{2-Furyl-(4-isopropyl-5-nitro)methyl}] piperazinyl]-phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 27)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[N-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 4-Isopropyl-5-nitro-2-furaldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm:7.45(d,1H,Ar-H),7.1(m,1H,Ar-H),6.9(m,1H,Ar-H),6.5(s,1H,Ar-H),6.0(m,1H,NH),4.77(m,1H,CH),4.5(m,1H,CH),4.0(m,3H,CH_2)3.8 (m,3H,CH_2), 3.2(m,4H,CH_2), 2.8(m,4H,CH_2),2.0(s,3H,CH_3).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-N-(4-t-butoxycarbonyl)piperazinyl-5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 102)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[N-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 4-N-(4-t-butoxycarbonyl)piperazinyl-5-nitro-2-thiophenaldehyde (J. Med. Chem., 2000, 43, 2258-2265, wherein instead of dimethyl amine hydrochloride, 1-(t-butoxycarbonyl)-piperazine was used) using Method B.

^{1}HNMR ($CDCl_3$) δppm:1.25-1.33 (s, 9H), 2.023 (s, 3H), 2.724 (s, 4H), 3.105 (s, 4H), 3.36-3.52 (d,4H), 3.60-54.0 (m, 9H), 4.75 (br s, 1H), 6.0 (br s, 1H), 6.592 (s, 1H), 6.937 (t, 1H), 7.0503 (d, 1H), 7.4 (dd, 1H).

BNSDOCID: <WO__03008389A1_I_>

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-N-piperazinyl-5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 103)

To a mixture of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-N-piperazinyl-5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide(0.15g) in dichloromethane (20 mL) at 0° C was added trifluoroacetic acid(2 ml). The resultant mixture was allowed to come to room temperature and was further stirred for 3 hours. It was then diluted with ethyl acetate (20 ml) and sodium carbonate (300 mg) was added and the mixture stirred for another for 10 min. The reaction mixture was filtered and the filterate evaporated *in vacuo* to give the title compound (Yield: 0.118g).

^{1}HNMR ($CDCl_5$ + DMSO) δppm: 1.96 (s, 3H), 2.59 (s, 4H), 2.88 (s, 4H), 3.16 (s, 4H), 3.35-3.36 (br s, 4H), 3.55-3.63 (m, 6H), 4.77 (br s, 1H), 6.86 (s, 1H0, 6.97 (s, 1H), 7.07-7.1 (d, 1H), 7.47 (s, 1H), 8.09 (br s, 1H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-N-(4-methyl) piperazinyl-5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl]-acetamide. (Compound No. 104)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[N-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 4-N-(4-methyl)-piperazinyl-5-nitro-2-thiophenaldehyde (prepared by following the method as described in J. Med. Chem., 2000, 43, 2258-2265), wherein 1-methyl-piperazine was used instead of dimethyl amine hydrochloride, using Method B.

^{1}HNMR ($CDCl_3$) ppm: 2.02 (s, 3H), 2.32 (s, 3H), 2.39- 557 (d, 4H), 2.65-52.8 (m,4H), 3.44 - 53.47 (s,4H), 3.60 (m, 3H), 3.9-3.95 (t, 2H), 4.05 (t, 1H), 4.77 (bs, 1H), 6.99 (bs, 1H), 6.59 (s , 1H), 691-6.97 (t, 1H), 7.05-7.07 (d,1H), 7.43-7.47 (d,1H).

Method C:

General Procedure:

Preparation of compound of Formula I wherein W is equal to C = O corresponding acid of Formula VII can be used and the amine of Formula VI can

BNSDOCID: <WO__03008389A1_I_>

be acylated through activated esters in the presence of condensing agents such as 1,3-dicyclohexylcarbodiimide (DCC) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC), along with 1-hydroxybenzotriazole (HOBT). Other methods of acylation can also be employed.

The following compounds were used using this method:

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl(5-methoxy)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 28)

To a mixture of (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide (1.14 mmol) and 5-methoxy-2-furoic acid (0.16 g, 1.14 mmol) and dry dimethylformamide (10 mL) at 5° C, N-methylmorpholine (0.14 g, 1.37 mmol) and 1-hydroxybenzo-triazole (0.17 g, 1.14 mmol) were added and stirred for 15 min. Next, 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (0.22 g, 1.14 mmol) was added to the above. The reaction mixture was allowed to come to room temperature and stirred for further 18 hours. It was then diluted with water and extracted with ethyl acetate (3 x 20 ml). The organic layers were dried over anhydrous sodium sulphate and evaporated *in vacuo*. The crude product was purified by column chromatography (3% MeOH/CH_2Cl_2) to get 0.37 g of product. The product was then digested with ether and filtered to yield 0.25 g of the title compound.

^{1}HNMR ($CDCl_3$) δppm: 7.43 (d, 1H), 7.04 (m, 2H), 6.92 (t, 1H), 6.03 (m, 1H), 5.31 (s, 1H), 4.75 (m, 1H), 3.91 (m, 7H), 3.8-3.51 (m, 3H), 3.09 (m, 4H), 2.02 (s, 3H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(5-acetamido)}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 29)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-acetamido-2-thiophenoic acid using Method C.

^{1}HNMR ($CDCl_3$ + DMSO) ppm: 10.81 (s, 1H), 7.69-6.60 (m, 6H), 4.75 (m, 1H), 4.01-3.57 (m, 8H), 3.08 (m, 4H), 2.17 (s, 3H), 1.98 (s, 3H)

BNSDOCID: <WO 03008389A1_I_>

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-pyrazolecarbonyl-(4-nitro)}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 30)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 4-nitro-pyrazole-3-carboxylic acid using Method C.

^{1}HNMR ($CDCl_3$ + DMSO) δppm: 8.3-6.6 (m, 6H), 4.74 (m, 1H), 4.1-2.1 (m, 12H+DMSO), 1.99 (s, 3H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-pyrazolecarbonyl(5-nitro)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 31)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-pyrazole-3-carboxylic acid using Method C.

^{1}HNMR ($CDCl_3$ + DMSO) δppm: 8.04 (t, 1H), 7.5 (dd, 1H), 7.13 (m, 2H), 6.9 (t, 1H), 4.78 (m, 1H), 4.1-3.25 (m, 8H), 3.13 (m, 4H+DMSO), 1.97 (s, 3H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(5-tert-butoxy-carboxamido)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide. (Compound No. 32)

The title compound was prepared with (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-tert-butoxycarboxamido-2-thiophenoic acid using Method C.

^{1}HNMR ($CDCl_3$) δppm: 7.5-6.75 (m, 4H), 6.46 (m, 1H), 6.16 (t, 1H), 4.76 (m, 1H), 4.2-3.25 (m, 8H), 3.07 (m, 4H), 2.02 (s, 3H), 1.53 (s, 9H)

Preparation of 5-tert-butoxycarboxamido-2-thiophenoic acid

(a) Ethyl 5-bis-tert-butoxycarboxamido-thiophene-2-carboxylate:

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To a mixture of ethyl 5-amino-thiophene-2-carboxylate (2.06 g, 12 mmol) in dry tetrahydrofuran at 5° C, sodium hydride (60% w/w, 0.58 g) was added and stirred for 10 minutes. Next, di-t-butoxypyrocarbonate (3.15 g, 14.5 mmol) was added and the reaction mixture stirred for 17 hrs. It was then diluted with ethyl acetate (200 ml) and washed with water. The organic layers were dried over anydrous sodium sulphate and evaporated *in vacuo*. The crude product was purified by column chromatography to yield 2.3 g of product.

^{1}HNMR (DMSO) δppm: 7.63 (d, 1H), 6.97 (d, 1H), 4.29 (q, 2H), 1.43 (s, 18H), 1.39 (t, 3H); M+1=394

(b) 5-tert-butoxycarboxamido-2-thiophenoic acid:

To ethyl 5-bis-tert-butoxycarboxamido-thiophene-2-carboxylate (0.27 g, 1 mmol) in tetrahydrofuran(15 ml), a solution of lithium hydroxide hydrate (0.1 g, 2.4 mmol) in water (5 mL) was added and the reaction mixture stirred for 24 hours. Another 0.1g of lithium hydroxide hydrate was added and the reaction mixture stirred for further 3 days. It was then acidified with saturated citric acid solution to pH=3. The mixture was extracted with ethyl acetate (3 x 30 ml). The organic layers were washed with water and brine solution, dried over anhydrous sodium sulphate and evaporated *in vacuo*. The product was digested with hexanes and filtered. The filtered solid was further digested with ether and filtered again. The filterate was evaporated to get the title compound.

^{1}HNMR (DMSO) δppm: 12.15 (br, 1H), 10.91 (s , 1H), 7.46 (d, 1H), 6.52 (d, 1H), 1.48 (s, 9H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl(5-trifluoroacetamido)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide. (Compound No. 33)

A mixture of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(5-tert-butoxy-carboxamido)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide (Compound No.32) (0.25 g) and 20% trifluoroaceticacid (10 ml) in

BNSDOCID: <WO 03008389A1 I >

dichloromethane was kept at 4-10^{0}C for 24 hours.The reaction mixture was then evaporated *in vacuo* and cooled to get the title compound .

^{1}HNMR ($CDCl_3$) δppm: 12.96 (s, 1H), 8.25 (m, 1H), 7.5-6.8 (m, 5H), 4.7 (m, 1H), 3.03 (m, 4H), 1.83 (m, 3H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl(5-amino)}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 34)

Compound No. 32 was treated with 20% trifluoroaceticacid in dichloromethane for 3 hrs and evaporated. The residue was then taken in acetone and treated with potassium carbonate (10 eq.), stirred for 15 min and filtered. Filterate was evaporated in vacuo. The residue was digested with ether and decanted to give the title compound along with potassium salt of trifluoroacetic acid.

^{1}HNMR (DMSO) δppm : 8.26 (m, 1H), 7.47 (m, 1H), 7.3-6.8 (m, 3H), 6.29 (s, 2H), 5.83 (m, 1H), 4.7 (m, 1H), 4.05 (m, 1H), 3.7 (m, 4H), 2.9 (m, 4H), 1.8 (m, 3H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl{5-(4-chloro-2-nitro-)-phenyl}}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide. (Compound No. 35)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-(4-chloro-2-nitro)-2-furoic acid using Method C

^{1}HNMR ($CDCl_3$) δppm:8-6.5 (m, 9H+$CDCl_3$), 4.78 (m, 1H), 4.1-3.5 (m, 8H), 3.13 (m, 4H), 2.0 (s, 3H)

BNSDOCID: <WO 03008389A1 I >

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl-(3-methyl)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 36)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 3-methyl-2-furoic acid using Method C.

^{1}HNMR ($CDCl_3$) δppm: 7.49 (dd, 1H), 7.34 (s, 1H), 7.06 (m, 1H), 6.97 (t, 1H), 6.34 (s, 1H), 6.06 (m, 1H), 4.76 (m, 1H), 4.1-3.75 (m, 8H), 3.11 (m, 4H), 2.29 (s, 3H), 2.02 (s, 3H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl-(3-methyl-5-nitro)}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 37)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 3-methyl-5-nitro-2-furoic acid using Method C.

^{1}HNMR ($CDCl_3$) ppm: 7.55 (dd,1H), 7.22 (s, 2H), 7.1 (dd, 1H), 6.23 (t, 1H), 4.79 (m, 1H), 4.1-3.2 (m, 12H), 2.36 (s, 3H), 2.03 (s, 3H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(4-dimethylamino-5-nitro)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 38)

The title compound was prepared reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 4-dimethylamino-5-nitro-2-thiophenoic acid using Method C

^{1}HNMR ($CDCl_3$) δppm: 7.45 (m, 1H), 7.09 (m, 1H), 6.92 (m, 2H), 5.99 (m,1H), 4.76 (m, 1H), 4.02 (t, 1H), 3.9-3.4 (m, 9H), 3.1 (m, 10 H), 2.04 (s, 3H)

M+1=535

BNSDOCID: <WO_ 03008389A1_I. >

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-Furoyl –(5-nitro)acrylic}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 39)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-2-furoylacrylic acid (J. Med. Chem., 16, 72-78, 1973) using Method C.

^{1}HNMR ($CDCl_3$) δppm:7.6(d,1H,Ar-H),7.4(m,1H,Ar-H),7.2(m,3H,Ar-H),6.8(d,1H,Ar-H),6.0(m,1H,NH),4.7(m,1H,CH),4.0(m,4H,CH_2),3.8(m,4H,CH_2),3.4(m,4H,CH_2),2.0(s,3H,CH_3).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl –(5-nitro)acrylic}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide. (Compound No. 40)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 2-thiophenoyl-5-nitroacrylic acid using Method C.

^{1}HNMR ($CDCl_3$) δppm: 7.9(d,1H,Ar-H),7.8(d,1H,Ar-H),7.6(d,1H,Ar-H),7.2(m,1H,Ar-H),7.0(m,2H,Ar-H),6.9(d,1H,Ar-H),6.0(m,1H,NH),4.78(m,1H,CH),3.8-3.6(m,8H,CH_2),3.2(m,4H,CH_2),2.0(s,3H,CH_3).

Preparation of Iodide (S)-N-[[3-[3-Fluoro-4 [N-1 [4-N-methyl-4-{2-furyl (5-nitro) methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl] acetamide. (Compound No. 41)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4 [N-1 [4-N-methyl-4-{2-furyl (5-nitro) methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl] acetamide and Iodomethane.

^{1}HNMR ($CDCl_3$) δppm: 8.1 (m, 1H, NH), 8.0 (m, 1H, Ar-H), 7.6 (m, 1H, Ar-H), 7.4 (d, 1H, ArH), 7.2 (m, 2H, Ar-H), 5.0 (m, 2H, CH_2), 4.7 (m, 1H, CH_2), 4.1 (t, 1H, CH), 3.3-3.6 (m, 3H, CH_2), 3.2 (broad, s, CH_3), 3.0 (m, 4H, CH_2) 2.8 (m, 4H, CH_2), 1.9 (s, 3H, CH_3)

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Example 2

Analogues of (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]- fluoroacetamide (Core II)

Preparation of (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]- fluoroacetamide (Core II)

(a) (S)-N-[[3-[3-Fluoro-4-[N-1-(4-tert-butoxycarbonyl)piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]fluoroacetamide:

To a mixture of (S)-[N-3-[3-Fluoro-4-[N-1-(4-tert-butoxycarbonyl) piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methylamine (1g, 2.5 mmol; US patent No. 5,700,799) and dry dimethylformamide (20 mL) at 5 °C were added fluoroacetic acid (0.2 g, 2.5 mmol), N-methylmorpholine (0.33g, 3 mmol) and 1-hydroxybenzotriazole (0.38 g, 2.8 mmol), and stirred the reacion mixture for 15 min. Then, 1-(3-dimethylaminopropyl)-3-ethycarbodimide hydrochloride (EDC) (0.48 g, 2.5 mmol) was added to the above,and it was further stirred for 20 hrs at room temperature. Water was added to the reaction mixture and it was then extracted with ethyl acetate. The combined organic layer were dried over anhydrous sodium sulphate and evaporated in vacuo. The crude product was purified by column chromatography to yield 0.38 g of product.

^{1}HNMR ($CDCl_3$) ppm: 7.45 (dd, 1H), 7.08 (m, 1H), 6.91 (m, 2H), 4.8 (d and m, 3H), 4.06 (t, 1H), 3.9-3.3 (m, 8H), 2.98 (m, 4H), 1.48 (s, 9H)

M+1 = 455

(b) (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl] methyl]- fluoroacetamide

To a mixture of (S)-N-[[3-[3-Fluoro-4-[N-1-(4-tert-butoxycarbonyl) piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]fluoroacetamide (0.25 g, 0.55 mmol) and dichloromethane (4 mL), trifluoroacetic acid (1 mL) was

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added and stirred for 2 hrs. The solvent was evaporated and to the reaction mixture was added acetone (10 mL),and potassium carbonate (0.5 g). This was further stirred for 15 min. The separated solid was filtered and the filtrate was evaporated in vacuo. The residue was used as such in subsequent step without further purification.

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-nitro)methyl}] piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-fluoroacetamide. (Compound No. 42)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]- fluoroacetamide and 5-nitro-2-furaldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.5-6.5 (m, 6H), 5-4.6 (m, 3H), 4.1-3.5 (m, 6H), 3.08 (m, 4H), 2.72 (m, 4H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen(5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]fluoroacetamide. (Compound No. 43)

The title compound was prepared with (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-fluoroacetamide and 5-nitro-2-thiophenaldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.81 (d, 1H), 7.43 (dd, 1H), 7.06 (m, 1H), 6.94 (m, 2H), 6.81 (m, 1H), 4.5-5 (m, 3H), 4.2-3.5 (m, 6H), 3.13 (s, 4H), 2.77 (s, 4H)

Example 3

Analogues of (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-difluoroacetamide (Core III)

Preparation of (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-difluoroacetamide (Core III) was similar to the method used for the synthesis of (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-

BNSDOCID: <WO_03008389A1_I_>

oxazolidinyl]methyl]-fluoroacetamide (Core II) except using difluoro acetic acid instead of fluoroacetic acid.

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen(5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]difluoroacetamide. (Compound No. 44)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-difluoroacetamide and 5-nitro-2-thiophenaldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.8 (d, 1H), 7.42 (dd, 1H), 7.05 (m, 1H), 6.9 (m, 3H), 5.93 (t, 1H), 4.8 (m, 1H), 4.08 (t, 1H), 3.9-3.5 (m, 6H), 3.12 (m, 4H), 2.73 (m, 4H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-difluoroacetamide. (Compound No. 45)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]-difluoroacetamide and 5-nitro-2-furaldehyde using Method B.

^{1}HNMR ($CDCl_3$) ppm: 7.5-6.75 (N, 5H+CHCl3 in $CDCl_3$), 6.51 (m, 1H), 5.94 (t, 1H), 4.81 (m, 1H), 4.2-3.3 (m, 6H), 3.1 (m, 4H), 2.7 (m, 4H)

Example 4

Analogues of (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]-methyl]-monochloroacetamide (Core IV)

Preparation of (S)-N-[[3-[3-Fluoro-4 (N-1-piperazinyl)-phenyl]]-2-oxo-5 oxazolidinyl]methyl]mono chloro acetamide (Core IV) was similar to the synthesis of (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)-phenyl[]-2-oxo-5-oxazolidinyl]-methyl]-fluoro-acetamide (core II) using chloroacetic acid instead of fluoroacetic acid.

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Preparation of (S)-N-[[3-[3-Fluoro-4 [N-1 [4-{2-furyl (5-nitro)methyl}] piperazinyl]phenyl]]-2-oxo-5-oxazolidinyl]methyl]mono chloro acetamide. (Compound No. 46)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4 [N-1-]piperazinyl]-phenyl]]-2-oxo-5 oxazolidinyl]methyl]mono chloro acetamide and5-nitro-2-furaldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.6 (d, 2H, Ar-H), 6.8 (7.3 (m, 4H, Ar-H), 6.6 (broad S, 1H, Ar-H), 4.7 (m, 1H, CH), 4.0 (m, 3H, CH_2Cl, CH) 3.8 (m, 5H, CH_2) 3.4 (m, 4H, CH_2), 2.8 (m, 4H, CH_2), 2.0 (s, 3H, CH_3).

IR: 1749, 1678 cm^{-1}.

Preparation of (S)-N-[[3-[3-Fluoro-4 [N-1 [4-[2-thiophenyl-(5-nitro)methyl]] piperazinyl]-phenyl]]2-oxo-5-oxazolidinyl]methyl] monochloroacetamide. (Compound No. 47)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4 [N-1-piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl] monochloroacetamide and 5-nitro-2-thiophene aldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.8 (d, 1H, Ar-H), 7.4 (d, 1H, Ar-H), 7.0 (m, 2H, Ar-H), 6.9 (m, 2H, ArH), 4.79 (m, 1H, CH) 4.0 (m, 3H, CH_2), 3.6-3.8 (m, 5H, CH_2), 3.2 (m, 2H, CH_2), 2.8 (m, 2H, CH_2), 2.0 (s, 3H, CH_3)

Preparation of (S)-N-[[3-[3-Fluoro-4 [N-1 [4-[2-thiophenyl-(4bromo-5-nitro) methyl]]piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl] monochloroacetamide. (Compound No. 48)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4 [N-1-piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl] monochloroacetamide and 4-bromo-5-nitro-2 thiophene aldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm:7.46(d,1H,Ar-H),7.0(m,2H,Ar-H),6.9(m,2H,Ar-HandNH),4.79(m,1H,CH),4.1(m,3H,CH_2),3.8(m,5H,CH_2), 3.2(m,4H,CH_2), 2.8(m,4H,CH_2)

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Example 5

Analogues of (S)-N-[[3-[3-Fluoro-4 (N-1-piperazinyl)-phenyl]2-oxo-5-oxazolidinyl]methyl] –2-chloropropionamide (Core V)

Preparation of (S)-N-[[3-[3-Fluoro-4 (N-1-piperazinyl)-phenyl]]-2-oxo-5 oxazolidinyl]methyl]-2-chloro propionamide (Core V) was similar to the synthesis of (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)-phenyl]]-2-oxo-5-oxazolidinyl]-methyl]-fluoroacetamide (core II) except using 2-chloropropionic acid instead of fluoroacetic acid.

Preparation of (S)-N-[[3-[3-Fluoro-4 [N-1 [4-[2-thiophenyl-(5-nitro)methyl]] piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl] –2-chloropropionamide. (Compound No. 49)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4 (N-1-piperazinyl)-phenyl]2-oxo-5-oxazolidinyl]methyl] –2-chloropropionamide and 5-nitro- -2 thiophene aldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.8(d,1H,Ar-H),7.4(d,1H,Ar-H),7.1(m,2H,Ar-H),6.9(m,2H,Ar-H,NH),4.8(m,1H,CH), 4.4(m,1H,CH),4.0(m,1H,CH),3.8-3.6(m,5H,CH_2), 3.2 (m,2H, CH_2), 2.8(m,2H,CH_2), 1.8(d,3H,CH_3).

IR 1752,1658 cm^{-1}.

Preparation of (S)-N-[[3-[3-Fluoro-4 [N-1 [4-[2-Furyl-(5-nitro)methyl]] piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl]–2-chloropropionamide. (Compound No. 50)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4 [N-1-piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl] –2-chloropropionamide and 5-nitro- 2-furfural using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.6(d,1H,Ar-H),7.4(d,2H,Ar-H,NH), 7.1(m,2H,Ar-H),6.9(m,1H,NH),6.6(broad s,1H,Ar-H),4.8(m,1H,CH), 4.4(m,1H,CH),4.0(m,1H,CH),3.8-3.6(m,5H,CH_2),3.2(m,2H,CH_2),2.8(m,2H,CH_2), 1.8(d,3H,CH_3).

IR 1745,1663 cm^{-1}.

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Preparation of (S)-N-[[3-[3-Fluoro-4 [N-1 [4-[2-thiophenyl-(4-bromo-5-nitro)methyl]]piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl] –2-chloropropionamide. (Compound No. 51)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4 [N-1-piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl] –2-chloropropionamide and 4-bromo-5-nitro-2-thiophene carboxaldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.46 (d,1H,Ar-H), 7.05-6.9 (m,3H,Ar-H), 4.78 (m,1H,CH), 4.4 (m,1H,CH), 4.0 (m,1H,CH),3.8 (m,4H,CH_2), 3.6 (m,2H,CH),3.11 (m,4H,CH_2),2.75 (m,4H,CH_2), 1.8 (m,3H,CH_3).

Example 6

Analogues of (S)-N-[[3-[3-Fluoro-4-(N-1-homopiperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide.

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-nitro) methyl}] homopiperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 52)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-homopiperazinyl)-phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-2-chloromethylfuran using Method A.

^{1}HNMR ($CDCl_3$) δppm: 7.43 (d, 1H), 7.25-6.75 (m, 2H), 6.58 (s, 1H), 6.15 (m, 1H), 4.87 (m, 1H), 4.25-3.0 (m, 10H), 2.9 (m, 4H), 2.1 (s, 3H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-{4-(3-furoyl)}homopiperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 53)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-homopiperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 3-furoic acid using Method C.

^{1}HNMR ($CDCl_3$) δppm: 7.8-7.25 (m, 3H+CHCl3 in $CDCl_3$), 7.05 (m, 1H), 6.93 (t, 1H), 6.56 (m, 1H), 6.11 (m, 1H), 4.8 (m, 1H), 4.2-3.1 (m, 12H), 2.07 (m, 5H).

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Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(5-nitro)}] homopiperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 54)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-homopiperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-2-thiophenoic acid using Method C.

^{1}HNMR ($CDCl_3$) δppm: 7.79 (m, 1H), 7.4 (m, 1H), 7.01 (m, 2H), 6.88 (t, 1H), 6.12 (m, 1H), 4.77 (m, 1H), 4.1-3.25 (m, 12H), 2.03 (s, 5H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl(5-nitro)}]homopiperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 55)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(N-1-homopiperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-2-furoic acid using Method C.

^{1}HNMR ($CDCl_3$) δppm: 7.5-6.75 (N, 5H+CHCl3 in $CDCl_3$), 5.99 (m, 1H), 4.76 (m, 1H), 4.1-3.25 (m, 12H), 2.2 (m, 2H), 2.03 (s, 3H)

Example 7

Analogues of (S)-N-[[3-[3-Fluoro-4-{N-1-(2-methyl)piperazinyl}phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide

Preparation of (S)-N-[[3-[3-Fluoro-4-{N-1-(2-methyl)piperazinyl}phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide

(a) Preparation of 2-methyl-4-tert-butoxycarbonylpiperazine.

To a solution of 2-methylpiperazine (5g, 0.05 mol) in water (30 mL),and tetrahydrofuran (60 mL) ,tert-butoxydicarbonate (4.35 g, 0.02 mol) were added and stirred for 2 days. The reaction mixture was subjected to

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vacuum until all the tetrahydrofuran was removed. The aqueous phase was then extracted with ethyl acetate (3 x 250 mL). The combined organic layer were washed with saturated sodium chloride solution, dried over anhydrous sodium sulphate and evaporated in vacuo to yield 3.2 g of the title compound.

^{1}HNMR ($CDCl_3$) δppm: 3.92 (br s, 2H), 2.96 (dd, 1H), 2.71 (m, 3H), 2.39 (m, 1H), 1.46 (s, 9H), 1.03(d, 3H).

M+1= 201

(b) Preparation of 1-(2-fluoro-4-nitrophenyl)-2-methyl-4-tert-butoxycarbonyl-piperzine

To a mixture of 2-methyl-4-tert-butoxycarbonylpiperazine (A, 1g, 0.005 mol) and DMSO (20 mL), 3,4-difluornitrobenzene (0.79 g, 0.005 mol), and potassium carbonate (3.45 g, 0.025 mol), were added and the reaction mixture heated to 120 °C for 8 hrs. It was then diluted with ethyl acetate and washed with water (3x) and brine solution. Combined organic layer were dried over anhydrous sodium sulphate and evaporated in vacuo to get a semisolid . This was further purified by column chromatography using 6 - 10% Hexane-ethyl acetate as eluent to yield 0.98 g compound.

^{1}HNMR ($CDCl_3$) δppm: 7.93 (m, 2H), 6.89 (t, 1H), 3.98 (m,2H), 3.8 (d, 1H), 3.4 (m, 2H), 3.15 (m, 2H), 1.49 (s, 9H), 1.1 (d, 3H)

(c) Preparation of 3-Fluoro-4-{N-1(2-methyl-4-tert-butoxycarbonyl) piperazinyl}-aniline.

To a solution of 1-(2-fluoro-4-nitrophenyl)-2-methyl-4-tert-butoxycarbonylpiperzine (B, 23 g) and methanol (100 mL), 10% palladium/carbon (5 g) was added and shaken in a Parr hydrogenation apparatus under 40 psi of hydrogen gas for 3 hrs. Then the reaction mixture was filtered over celite and the filtrate evaporated in vacuo to yield 17.2 g of the final product.

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^{1}HNMR ($CDCl_3$) δppm: 6.88 (t, 1H), 6.4 (m, 2H), 4-2.75 (m, 9H), 1.46 (s, 9H), 0.85 (d, 3H)

M+1= 311

(d) Preparation of N-Benzyloxycarbonyl-3-fluoro-4-{N-1-(2-methyl-4-tert-butoxylcarbonyl)-piperazinyl}-aniline.

To a mixture of 3-Fluoro-4-{N-1(2-methyl-4-tert-butoxycarbonyl) piperazinyl}aniline (C, 17 g, 0.055 mol) and THF (200 ml) at 5° C, sodium bicarbonate (23 g, 0.274 mol), was added . Benzylchloroformate (11.22g, 0.066 mol) was added dropwise to the above. The reaction mixture was allowed to come to room temperature and was further stirred for 18 hrs. It was then filtered and evaporated in vacuo. The residue was dissolved in ethyl acetate and washed with saturated sodium bicarbonate solution, water and brine water. The combined organic layer were dried over anhydrous sodium sulphate and evaporated in vacuo to give 27 g of final product.

^{1}HNMR ($CDCl_3$) δppm: 7.33 (m,6H), 6.97 (m, 2H), 6.78 (m,1H), 5.17 (s, 2H), 3.8-2.7 (m,7H), 1.47 (s, 9H), 0.88 (d, 3H)

M+1=444, M+2=445

(e) Preparation of (R)- [N-3-[3-Fluoro-4-[N-1-(2-methyl-4-tert-butoxycarbonyl)-piperazinyl]-phenyl]-2-oxo-5-oxazolidinyl]methanol

To a solution of N-Benzyloxycarbonyl-3-fluoro-4-{N-1-(2-methyl-4-tert-butoxylcarbonyl)-piperazinyl}-aniline (D, 25 g, 0.056 mol) in dry tetrahydrofuran (150 mL), at 78°C, butyl lithium(49.2 mL, 15% sol. In hexane, 0.112 mol) was added under positive pressure of nitrogen. The reaction mixture was stirred at -78° C for 1.5 hrs. R-glycidyl butyrate (9.71 g, 0.067 mol) was added to the above and the reaction mixture was stirred at –78°C for 1hr further the reaction mixture was allowed to come to room temperature and stirred for further 18 hrs. 100 mL of saturated ammonium chloride solution was added to the above and the reaction mixture

BNSDOCID: <WO 03008389A1 I >

extracted with ethyl acetate. The combined organic layers was washed with water and brine solution, dried over anhydrous sodium sulphate and evaporated in vacuo. The crude product was purified by column chromatography using 3% (MeOH/$CHCl_3$) as eluent to yield 8.8 g of final product.

^{1}HNMR ($CDCl_3$) δppm: 7.33 (m, 1H), 7.15 (m,1H), 6.99 (t, 1H), 4.75 (m,1H), 4.1-3.75 (m,11H), 1.49 (s, 9H), 0.92 (d, 3H)

M+1=410

(f) Preparation of (R)-[N-3[3-Fluoro-4-[N-1-(2-methyl-4-tert-butoxycarbonyl)-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl methanesulfonate.

To a solution of (R)-[N-3-[3-Fluoro-4-[N-1-(2-methyl-4-tert-butoxycarbonyl)-piperazinyl]-phenyl]-2-oxo-5-oxazolidinyl]methanol (E, 6.5 g, 0.016 mol) in dichloromethane (200 mL) 5° C, triethylamine (2.4 g, 0.024 mol) and methanesulfonylchloride (2.66 g, 0.024 mol) were added and the reaction mixture was stirred for 17 hr. The reaction mixture was then diluted with dichloromethane and washed with saturated sodium bicarbonate solution and brine water. The combined organic layer was dried over ahydrous sodium sulphate and evaporated in vacuo to yield 6.5 g of product.

^{1}HNMR ($CDCl_3$) δppm: 7.38 (m, 2H), 7.11 (m,1H), 4.91 (m, 1H), 4.75-2.5 (m,14H), 1.48 (s, 9H), 0.76 (m, 3H)

M+1=488

(g) Preparation of (R)-[N-3[3-Fluoro-4-[N-1-(2-methyl-4-tert-butoxycarbonyl)-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl] methylazide.

To a solution of (R)-[N-3[3-Fluoro-4-[N-1-(2-methyl-4-tert-butoxycarbonyl)piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl

BNSDOCID: <WO_03008389A1_I_>

methanesulfonate compound (F, 6.5 g, 0.013 mol) in dimethylformamide (200 mL), sodium azide (4.33g, 0.067 mol) was added and the reaction mixture heated to 80° C for 7 hrs. The solid was filtered off and the filterate evaporated in vacuo. The residue was dissolved in chloroform and washed with water and brine solution. The combined organic layer was dried over anhydrous sodium sulphate and evaporated in vacuo to yield 6 g of the product.

^{1}HNMR ($CDCl_3$) δppm: 7.38 (m,1H), 7.13 (m,1H), 7.01 (m,1H), 4.77 (m,1H), 4.25-3 (m,11H), 1.47 (s,9H), 0.76 (d, 3H)

(h) Preparation of (S)-[N-3-[3-Fluoro-4-[N-1-(2-methyl-4-tert-butoxycarbonyl)-piperazinyl]-phenyl]-2-oxo-5-oxazolidinyl] methylamine.

To a solution of (R)-[N-3[3-Fluoro-4-[N-1-(2-methyl-4-tert-butoxycarbonyl)piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methylazide (G, 6 g) in methanol (100 mL), 10% palladium/carbon (0.6 g) was added and the reaction mixture shaken in a Parr hydrogenation apparatus under 40 psi hydrogen pressure for 9 hrs. The reaction was filtered over celite and the filterate evaporated in vacuo to yield 5 g of product. The crude product was used in further next reaction without further purification.

^{1}HNMR ($CDCl_3$) δppm: 7.44 (m, 1H), 7.14 (m, 1H), 7.00 (m,1H), 4.67 (m, 1H), 4.25-2.75 (m,11H), 1.48 (s, 9H), 0.79 (d, 3H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-(2-methyl-4-tert-butoxycarbonyl)-piperazinyl]phenyl]2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 56)

To a solution of (S)-[N-3-[3-Fluoro-4-[N-1-(2-methyl-4-tert-butoxycarbonyl) piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methylamine (H, 5 g, 0.0122 mol) in dichloromethane (150 mL), pyridine (1.94 g, 0.025 mol) and acetic anhydride (2.5 g, 0.025 mol) were added and the reaction mixture was stirred at room temperature for 17 hrs. The reaction mixture was diluted with dichloromethane

BNSDOCID: <WO 03008389A1 I >

and washed with saturated sodium bicarbonate solution and brine water. The combined organic layer was dried over anhydrous sodium sulphate and evaporated in vacuo. The residue obtained was purified by column chromatography to yield 3.5 g of final product.

^{1}HNMR ($CDCl_3$) ppm: 7.4 (d, 1H), 7.07 (d, 1H), 6.99 (t, 1H), 6.18 (m, 1H), 4.76 (m,1H), 4.06 (t, 1H), 3.9-2.6 (m, 10 H), 2.01 (s, 3H), 0.89 (d, 3H)

HPLC: 84% purity

(j) Preparation of (S)-N-[[3-[3[Fluoro-4-{N-1-(2-methyl)piperazinyl}phenyl]-2-oxo-5-oxazolidinyl]methyl acetamide

To a solution of (S)-N-[[3-[3-Fluoro-4-[N-1-(2-methyl-4-tert-butoxycarbonyl)piperazinyl]phenyl]2-oxo-5-oxazolidinyl]methyl]acetamide (I, 0.5g, 1.11 mmol) in dichloromethane (8 mL), trifluoroacetic acid (2 mL) was added and stirred for 2 hrs. The reaction mixture was then evaporated and dried in vacuo. The residue was taken in acetone (10 mL), potassium carbonate (0.78 g, 5.55 mmol) was added to it and stirred for 15 minutes. Then the reaction mixture was fitered and the filterate evaporated in vacuo to yield the product in quantitative yield. This product was used as such in next step without further characterization.

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[2-methyl-4-{2-thiophen-(5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 57)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-{N-1-(2-methyl)piperazinyl}phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-2-thiophene aldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.8 (s, 1H), 7.39 (dd, 1H), 7.06 (m, 2H), 6.89 (m, 1H), 6.02 (m, 1H), 4.76 (m, 1H), 4.03 (t, 1H), 3.8-2.25 (m, 12H), 2.02 (s, 3H), 0.96 (d, 3H)

BNSDOCID: <WO__03008389A1_I_>

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[2-methyl-4-{2-furyl(5-nitro)methyl}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 58)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-{N-1-(2-methyl)piperazinyl}phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-2-furaldehyde using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.5-6.8 (m, 4H), 6.5 (s, 1H), 6.06 (m, 1H), 4.76 (m, 1H), 4.02 (t, 1H), 4.8-2.25 (m, 12H), 2.0 (s, 3H), 0.92 (d, 3H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[2-methyl-4-{2-furoyl-(5-nitro)}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 59)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-{N-1-(2-methyl)piperazinyl}phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-2-furoic acid using Method C.

^{1}HNMR ($CDCl_3$) δppm: 7.7-6.8 (m, 5H+CHCl3), 6.16 (m, 1H), 4.79(m, 1H), 4.2-2.8 (m, 11H), 2.03 (s, 3H), 1.00 (d, 3H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[2-methyl-4-{2-thiophenoyl-(5-nitro)}]- piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 60)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-{N-1-(2-methyl)piperazinyl}phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-2-thiophenoic acid using Method C.

^{1}HNMR ($CDCl_3$) δppm: 7.84 (d, 1H), 7.47 (dd, 1H), 7.21 (d, 1H), 7.11 (d, 1H), 7.04 (t, 1H), 5.97 (m, 1H), 4.75 (m, 1H), 4.2-2.75 (m, 11H), 2.02 (s, 3H), 0.96 (d, 3H)

Example 8

Analogues of (S)-N-[[3-[3-Fluoro-4-[N-1-{2,6-dimethyl-}-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core VIII)

BNSDOCID: <WO 03008389A1_I_>

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furoyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 61)

The title compound was prepared by reacting (S)-N-[[3-[3-fluoro-4-[N-1-[2,6-methyl]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 2-furoyl chloride using Method A.

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(5-formyl)methyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 62)

The title compound was prepared by reacting (S)-N-[[3-[3-fluoro-4-[N-1-[2,6-dimethyl]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-formyl-2-chloro methyl furan using Method A.

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(5-nitro)methyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 63)

The title compound was prepared by reacting (S)-N-[[3-[3-fluoro-4-[N-1-[2,6-dimethyl]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-furaldehyde using Method B.

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(5-hydroxymethyl)methyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 64)

The title compound was prepared with (S)-N-[[3-[3-fluoro-4-[N-1-[2,6-dimethyl]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-hydroxy methyl furan 2-carboxaldehyde using Method B.

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Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(aldoxime)methyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 65)

The title compound was prepared by reacting (S)-N-[[3-[3-fluoro-4-[N-1-[2,6-dimethyl]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-aldoxime-2-chloromethyl furan using Method A,

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-(2-thienylacetyl)]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 66)

The title compound was prepared reacting (S)-N-[[3-[3-fluoro-4-[N-1-[2,6-dimethyl]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and thiophene-2-acetyl chloride using Method A.

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(5-cyano)methyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 67)

The title compound was prepared by reacting (S)-N-[[3-[3-fluoro-4-[N-1-[2,6-dimethyl]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-cyano-2-chloromethyl furan using Method A

Example 9

Analogues of (S)-N-[[3-[3-Fluoro-4-[N-1-{3-methyl-}-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core IX)

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[3-methyl-4-{2-thiopheneacetyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 68)

The title compound was prepared by reacting (S)-N-[[3-[3-fluoro-4-[N-1-[3-methyl]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and thiophene-2-acetyl chloride using Method A.

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Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[3-methyl-4-{2-furoyl-(5-nitro)}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 69)

The title compound was prepared by reacting (S)-N-[[3-[3-fluoro-4-[N-1-[3-methyl]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro furan 2-carboxaldehyde using Method B.

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[3-methyl-4-{2-thienoyl-(5-nitro)}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 70)

The title compound was prepared by reacting (S)-N-[[3-[3-fluoro-4-[N-1-[3-methyl]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-thiophene-2-carboxaldehyde using Method B

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-methyl-2-furyl-(5-formyl)methyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 71)

The title compound was prepared by reacting (S)-N-[[3-[3-fluoro-4-[N-1-[3-methyl]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-formyl-2-chloromethylfuran using Method A

Preparation of (S)-N-[[3-[3-Fluoro-4-[4-{N-acetyl-N-2-furyl-(5-nitro)methyl}] aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 72)

The title compound was prepared by acetylation of (S)-N-[[3-[3-Fluoro-4-[4-{N-2-furyl-(5-nitro)methyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide with acetic anhydride and pyridine.

^{1}HNMR ($CDCl_3$) δppm:7.45(d,1H),7.28 , 6.96(m,3H), 6.52 (bs,1H), 6.00 (bs,1H), 4.77 (bs,1H), 4.57 (s,2H), 4.07-3.43 (m,5H), 2.80 (t,2H), 2.49 (s,3H), 2.04 (s,5H), 1.91-1.87 (m,3H).

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Example 10

Analogues of (S)-N-[[3-[3-Fluoro-4-[{3-methyl-4-(N-methyl-)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core X)

Preparation of (S)-N-{3-[4-[3-methyl,4-(N-methyl)amino piperidin-1-yl]-3-fluorophenyl]-2-oxo-oxazolidin-5-yl}methyl acetamide.

N-(2-methyl methacryl)benzylamine: To a solution of benzylamine(43.6ml,406.8mmol) in methanol(50ml) was added methyl methacrylate(64.52ml,644.4mmol). The reaction mixture was refluxed for 32 hours. Solvent was evaporated under reduced pressure and the residue was purified through column chromatography using hexane:ethylacetate(5%) as eluent to give 67gm of the desired product as oil.

^{1}HNMR($CDCl_3$):7.248(s,5H),3.776(S,2H),3.674(S,3H),2.834(m,1H),2.615&2.686(m,2H),1.676 (d,3H).

N,N'-[2-Carboethoxyethyl ,methyl(2-methyl)propionate]benzylamine:A mixture of N-(2-methylmethacryl) benzylamine methacrylate derivative (64gm, 309.1mmol)and ethylacrylate (35.6gm, 352.4 mmol) was heated at 80^0 C for 12 hours.The reaction mixtre was heated for further 5 hours. Ethylacrylate was removed under reduced pressure and the residue was purified by column chromatography using hexane: ethyl acetate(1%) as eluent (Yield-63gms).

^{1}HNMR($CDCl_3$):7.34-7.22(bs,5H),4.07(dd,2H)3.65(s,3H),3.52(q,2H),2.79-2.66(m,4H),2.45-2.36(m,3H),1.25(t,3H)

N-Benzyl-3-methyl piperidin-4-one: To a hot solution of benzene (590ml) was added sodium hydride (20gms, mmol). After 5 minutes ethyl alcohol (0.3ml) was added. The reaction mixture was heated at 80-90° C for 10 to 15min then benzylamine derivative (59gms) was added dropwise. Reaction mixture was then refluxed for 5 hrs. at 90° C.

BNSDOCID: <WO 03008389A1 I >

Reaction mixture was cooled down to room temperature and water was added slowly to decompose sodium hydride followed by addition of conc. hydrochloric acid. The aqueous layer was then separated and refluxed at 100 ° C for 6-8 hours. The aqueous solution was then added to solid potassium carbonate and extracted with ethyl acetate. Ethyl acetate layer was washed with water and dried over anhydrous sodium sulphate and solvent was removed to give 8.5gms of product.

^{1}HNMR($CDCl_3$):7.36-7.26(bs,5H),3.60(s,2H),3.11-3.05(m,2H),2.66-2.58(m,2H),2.45-2.37(m,2H),0.99(d,3H)

N-Benzyl 3-methyl piperidine-4-oxime: To a solution of N-benzylpiperidin-4-one derivative18.5gms) in pyridine (75ml) was added hydroxylamine hydrochloride (6.93gms). The reaction mixture was stirred at room temperature for 1hour then at 60 ° C for 2hr. Pyridine was removed under reduced pressure and the residue was digested with isopropyl alcohol and filtered. Yield-17.5gms as white solid. m.p. 221 ° C

^{1}HNMR($CDCl_3$):13.50(bs,1H),7.60-7.47(m,5H),4.15(s,2H),3.54-3.43(m,2H),2.79-2.43(m,4H),1.08(d,3H).

N-Benzyl-3-methyl-4-aminopiperidine:To a solution of the oxime derivative (35gm) in methanolic ammonia (250ml) was added Raney Ni (3.5gms). The whole reaction mixture was hydrogenated at 45psi for 6hours. The reaction mixture was filtered through celite bed and washed with methanol. Solvent was removed to give 25gms of product.

^{1}HNMR($CDCl_3$):7.43-7.31(bs,5H),3.74(bs,2H),3.61(s,2H),2.44-2.08(m,7H),0.99(bs,3H)

N-Benzyl-3-methyl-4-(t-butyloxycarbonyl)aminopiperidine:To a solution of 4-aminopiperidine derivative (8.0gm,39.2mmol) in dichloromethane (75ml) was added triethylamine (6.2ml) followed by addition of BOC-anhydride

BNSDOCID: <WO_03008389A1 I >

(dropwise,10.7ml, mmol) at 0° C. The reaction mixture was then stirred overnight at room temperature. The reaction mixture was washed with water 3 to 4 times. The organic layer was then separated and dried over anhydrous sodium sulphate and evaporated in vacuo. The residue was then dried to give desired product in 10.7gms as oil.

^{1}HNMR($CDCl_3$):7.35(bs,5H),2.85(s,2H),2.85-2.82(m,2H),2.40-2.02(bs,2H),2.06-1.90(m,4H),1.44(s,9H),0.90(d,3H).

N-(t-butyloxy)amino-3-methylpiperidine:To a solution of N-benzyl piperidine derivative (22gms,72.3mmol) in methanol (100ml) was added dry ammonium formate(6.8gms,108.5mmol) and Pd/C (10%,3.3gm). The reaction mixture was then refluxed for 6 to 8 hr. at 80° C. The reaction mixture was filtered through celite bed using methanol. Solvent was evaporated under reduced pressure. Residue was dried to give 15.0gms of desired product.

^{1}HNMR($CDCl_3$):3.80(bs,1H),3.08(m,1H),2.86(m,2H),2.66-2.61(m,2H),1.99-1.95(m,1H),1.67-1.45(m,2H),1.45(s,9H),0.91(d,3H).

1-[4(N-t-Butyloxycarbonylamino-3-methyl)piperidin1-1-yl]-3-fluoro]-nitrobenzene: To a solution of aminopiperidine derivative (15gm,70mmol) in acetonitrile (120ml) was added diisopropylethyl amine followed by the addition of 1,2-difluoro-4-nitrobenzene. The reaction mixture was refluxed for 5 to 6 hours. Thereafter, acetonitrile was evaporated from reaction mixture. The residue was dissolved in ethyl acetate, washed with water 3 to 4 times. The combined organic layers were dried over sodium sulphate and evaporated in vacuo to give 24gms(97%) of the desired product.

^{1}HNMR($CDCl_3$):7.97-7.87(m,2H),6.92-6.86(t,1H), 3.86 (bs,1H), 3.67 (t,1H), 3.35(m,1H),3.20-3.16(m,1H),2.94 (t,1H),2.63(t,1H),2.03-1.84(m,1H),1.68-1.57(m,1H),1.45(s,9H),1.01(d,3H)

BNSDOCID: <WO__03008389A1_I_>

The following compounds were also prepared:

1-[[3-methyl 4(N-t-butyloxycarbonyl,N-methyl)amino]piperidin-1-yl]-3-fluoro]-nitrobenzene,

1-[[3-methyl 4(N-t-butyloxycarbonyl,N-methyl)amino]piperidin-1-yl]-3-fluoro]-aniline,

1-{N-Carbobenzyloxy-[3-methyl 4(N-t-butyloxycarbonyl,N-methyl)amino]piperidin-1-yl]-3-fluoro]-aniline,

(S)-(N)-{3-[4-[3-methyl 4(N-t-butyloxycarbonyl,N-methyl)amino]piperidin-1-yl]-3-fluorophenyl]-2-oxo-oxazolidin-5-yl}methanol,

(S)-(N)-{3-[4-[3-methyl 4(N-t-butyloxycarbonyl,N-methyl)amino]piperidin-1-yl]-3-fluorophenyl]-2-oxo-oxazolidin-5-yl}methyl methanesulfonate,

(S)-(N)-{3-[4-[3-methyl 4(N-t-butyloxycarbonyl,N-methyl)amino]piperidin-1-yl]-3-fluorophenyl]-2-oxo-oxazolidin-5-yl}methyl azide,

(S)-(N)-{3-[4-[3-methyl 4(N-t-butyloxycarbonyl,N-methyl)amino]piperidin-1-yl]-3-fluorophenyl]-2-oxo-oxazolidin-5-yl}methyl amine,

(S)-(N)-{3-[4-[3-methyl 4(N-t-butyloxycarbonyl,N-methyl)amino]piperidin-1-yl]-3-fluorophenyl]-2-oxo-oxazolidin-5-yl}methyl acetamide,

(S)-(N)-{3-[4-[3-methyl 4(N-methyl)amino]piperidin-1-yl]-3-fluorophenyl]-2-oxo-oxazolidin-5-yl}methyl acetamide,

Preparation of (S)-N-[[3-[3-Fluoro-4-[{3-methyl-4-(N-methyl-N-thiophenacetyl)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide. (Compound No. 73)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[{3-methyl-4-(N-methyl-)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide and thiophene-2-acetyl chloride by method A.

^{1}HNMR ($CDCl_3$) ppm: 7.44-6.91 (m, 6H), 6.05 (bs, 1H), 4.77 (bs, 1H), 4.50-4.25 (m, 1H), 4.06-2.88 (m, 15H), 2.04 (s, 4H), 1.15 (s, 1H), 1.14 (d, 1H), 0.85-0.77 (m, 2H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[[3-methyl-4-{N-methyl-2-furoyl(5-nitro)}]-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 74)

BNSDOCID: <WO_03008389A1 I >

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[[3-methyl-4-{N-methyl-}]- aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide and 5-nitro-2-furoyl chloride by using Method A.

^{1}HNMR ($CDCl_3$) ppm: 7.48-7.06 (m, 4H), 6.22 (bs, 1H), 4.78 (bs, 1H), 3.03-4.02 (9H), 3.00-2.10 (m, 2H), 2.02 (s, 3H), 1.74 (bs, 4H), 0.80 (m, 3H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[[3-methyl-4-{N-methyl-2-thienoyl-(5-nitro)}]- aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 75)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[[3-methyl-4-{N-methyl-}]- aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide and 5-nitro-2-thiophenoyl chloride by using Method A.

^{1}HNMR ($CDCl_3$) δppm: 7.87-6.85 (m, 6H), 4.70 (bs, 1H), 3.94 (t, 1H), 3.74 (t, 1H), 3.55 (s, 2H), 3.50-2.50 (m, 12H), 1.94 (s, 3H), 0.75 (bs, 3H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[{3-methyl-4-(N-methyl-N-2-furoyl)}- aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 76)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[{3-methyl-4-(N-methyl-)}- aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide and 2-furoyl chloride by using Method A.

^{1}HNMR ($CDCl_3$) δppm: 7.46 (bs, 1H), 7.38 (m, 1H), 6.93 (d, 2H), 6.49 (bs, 1H), 6.02 (bs, 1H), 4.77 (bs, 1H), 4.52-4.25 (m, 1H), 3.99 (t, 1H), 3.77-3.49 (m, 5H), 3.20&3.16 (s, 3H), 2.99 (d, 1H), 2.82 (t, 1H), 2.65-2.17 (m, 4H), 2.02 (s, 3H), 0.87 (t, 3H).

BNSDOCID: <WO__03008389A1_I_>

Preparation of (S)-N-[[3-[3-Fluoro-4-[[3-methyl-4-{N-methyl-N-2-furyl (5-nitro)}]- aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide. (Compound No. 77)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[[3-methyl-4-{N-methyl}]- aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide and 5-nitrofuraldehyde by using Method B.

^{1}HNMR ($CDCl_3$) δppm: 7.39 (d,1 H), 7.06-6.88 (m, 2H), 6.48 (t, 1H), 6.17 (bs, 1H), 4.76 (bs, 1H), 4.01-3.25 (m, 8H), 2.60 (t, 1H), 2.33 (s, 4H), 2.01 (m, 1H), 1.84 (s, 5H), 1.66 (m, 3H), 0.88 (t, 2H), 0.8 (t, 1H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[[3-methyl 4-{N-methyl-N-2-thienyl-(5-nitro)}]-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 78)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[[3-methyl 4-{N-methyl-}]-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide and 5-nitro thiophene 2-aldehyde by using the Method B.

Example 11

Analogues of (S)-N-[[3-[3-Fluoro-4-[4-(N-ethyl)-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XI)

The preparation of (S)-N-[[3-[3-Fluoro-4-[4-(N-ethyl)-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XI) is similar to the synthesis of (S)-N-[[3-[3-Fluoro-4-[4-(N-methyl)-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XIII).

Preparation of (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-2-thienoyl-(5-nitro)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 79)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro –2-thienoyl chloride by using Method A.

BNSDOCID: <WO_03008389A1_I_>

^{1}HNMR ($CDCl_3$) δppm: 7.45 (d, 1H), 7.45 (d, 1H), 7.23 (d, 1H), 7.07-6.97 (m, 2H), 4.92 (bs, 1H), 3.98 (t, 1H), 3.98-3.47 (m, 9H), 2.76 (bs, 1H), 2.15 (m, 2H), 2.01 (s, 4H), 1.88 (d, 2H), 1.41 (bs, 3H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-2-furoyl-(5-nitro)} aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 80)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-}aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-2-furoyl chloride by using the Method A.

^{1}HNMR ($CDCl_3$) δppm: 8.01-6.96 (m, 5H), 6.05 (bs, 1H), 5.29 (s, 1H), 4.91 (m, 1H), 4.75 (bs, 1H), 4.27-3.99 (m, 1H), 3.77-3.49 (m, 7H), 2.95-2.32 (m, 3H), 2.02 (bs, 4H), 1.25 (bs, 3H)

Preparation of (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-N-2-furoyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 81)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 2-furoylchloride using Method A.

Preparation of (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-N-2-thiophenacetyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 82)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and thiophene-2-acetyl chloride by using Method A.

^{1}HNMR ($CDCl_3$) ppm: 7.46-6.92 (m, 6H), 6.18 (bs, 1H), 4.76 (bs, 1H), 4.58 (bs, 1H), 4.01-3.35 (m, 10H), 2.75-2.50 (m, 2H), 2.02 (s, 3H), 1.97-1.75 (m, 3H), 1.45 (m, 1H), 1.20 (s, 3H)

BNSDOCID: <WO__03008389A1_I_>

Preparation of (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-N-2-thiophenyl-(5-nitro) methyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide. (Compound No. 83)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-)methyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide and 5-nitro thiophene-2-aldehyde by using the Method B.

^{1}HNMR ($CDCl_3$) ppm: 7.79 (d, 1H), 7.43 (dd, 1H), 7.05 (dd, 1H), 6.92 (t, 1H), 6.83 (d, 1H), 6.05 (t, 1H), 4.75 (bs, 1H), 4.01 (t, 1H), 3.75 (s, 2H), 3.84-3.44 (m, 5H), 2.71-2.60 (m, 5H), 1.75-1.90 (m, 4H), 1.97 (s, 3H), 1.07 (t, 3H).

Example 12

Analogues of (S)-N-[[3-[3-Fluoro-4-(4-aminopiperidine-1-yl) phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XII)

The title core XII is prepared by following the procedure as given in WO 95/25106.

Preparation of (S)-N-[[3-[3-Fluoro-4-[4-{N-thienyl-(5-nitro)methyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 84)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(4-aminopiperidine-1-yl) phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-thiophene-2-aldehyde by using Method B.

Preparation of (S)-N-[[3-[3-Fluoro-4-[4-{2-furyl-(5-nitro)methylene}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 85)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4- [4 -aminopiperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-2-furaldehyde.

BNSDOCID: <WO_03008389A1_I_>

^{1}HNMR ($CDCl_3$) ppm: 8.2 (s, 1H, CH), 7.8 (t, 1H, NH), 7.6 (m, 1H, Ar-H), 7.4 (m, 1H, Ar-H), 6.8-7.0 (m, 2H, Ar-H), 4.7 (m, 1H, CH), 4.0 (t, 1H, CH), 3.4-3.8 (m, 7H, CH_2). 2.0 (s, 3H, CH_3), 2.0 (m, 2H, CH_2), 1.9 (m, 2H, CH_2)

IR: 1748, 1656 cm^{-1}

Preparation of (S)-N-[[3-[3-Fluoro-4-[4-{N-2-furyl-(5-nitro)methyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 86)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-(4-aminopiperidine-1-yl) phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-2-furaldehyde by using Method B.

^{1}HNMR ($CDCl_3$) ppm: 7.41-6.45 (m, 4H), 6.48 (bs, 1H), 6.11 (bs, 1H), 4.75 (bs, 1H), 4.04-3.97 (m, 1H), 3.95 (s, 2H), 3.76-3.57 (m, 3H), 3.40-3.37 (m, 2H), 2.75-2.67 (m, 3H), 2.01 (bs, 3H), 1.74 (bs, 3H), 1.66-1.55 (m, 2H)

Example 13

Analogues of (S)-N-[[3-[3-Fluoro-4-[4-{N-methyl-}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XIII)

Preparation of (S)-N-[[3-[3-Fluoro-4-[4-{N-methyl-N-2-pyrrole-(5-nitro)methyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 87)

The title compound was prepared by reacting Core XIII and 5-nitro-pyrrole-2-aldehyde using Method B.

^{1}HNMR ($CDCl_3$) ppm: 7.41 (d, 1H), 7.05 (d, 1H), 6.92 (t, 1H), 6.17-6.12 (m, 2H), 4.77-4.73 (m, 1H), 4.05-3.46 (m, 7H), 2.69-2.62 (t, 4H), 2.33 (s, 3H), 2.09 (s, 2H), 2.04 (s, 3H), 2.02-1.81 (m, 3H).

BNSDOCID: <WO__03008389A1_I_>

Preparation of (S)-N-[[3-[3-Fluoro-4-[4-{N-methyl-N-2-furyl-(5-acetoxymethyl)methyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 88)

The title compound was prepared by reacting Core XIII and 5-acetoxy-pyrrol-2-aldehyde using Method A.

^{1}HNMR ($CDCl_3$) ppm: 7.40 (d, 1H), 7.05 (d, 1H), 6.90 (t, 1H), 6.39 (bs, 1H), 6.09 (bs, 1H), 5.01 (s, 2H), 4.75 (bs, 1H), 4.02-3.96 (m, 3H), 3.75-3.46 (m, 5H), 2.90 (bs, 1H), 2.71-2.63 (t, 2H), 2.54 (s, 3H), 2.03 (s, 3H), 1.90 (s, 3H), 1.95-1.87 (m, 3H).

Preparation of (S)-N-[[3-[3-Fluoro-4-[4-{N-methyl-N-2-furoyl-(5-nitro)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 89)

The title compound was prepared from Core XIII and 5-nitro-2-furoyl chloride using Method A.

^{1}HNMR ($CDCl_3$) ppm:7.87-6.91(m,6H),4.76(bs,1H),

Example 14

Analogues of (S)-N-[[3-[3-Fluoro-4[N-1, 3-[N-methyl aminopyrolidinyl] phenyl]]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XIV)

Preparation of (S)-N-[[3-[3-Fluoro-4[N-1-[3-[N-methyl [N-{2-thiophenyl (5-nitro)methyl}] aminopyrodinyl]phenyl]]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 90)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4[N-1, 3-[N-methyl aminopyrodinyl]phenyl]]-2-oxo-5-oxazolidinyl]methyl]acetamide (WO 95/25106) and 5-nitro-2-thiophenecarboxaldehyde using MethodB.

^{1}HNMR ($CDCl_3$) ppm: 7.8 (d, 1H, Ar-H), 7.5 (d, 1H, Ar-H), 7.0 (m, 2H, Ar-H), 6.8 (t, 1H, Ar-H), 6.4 (t-1H, NH), 4.7 (m, 1H, CH), 4.0 (t, 1H, CH), 3.4-3.8 (m, 9H, CH_2), 2.4 (s, 3H, CH_3), 2.3 (m, 1H, CH), 2.1 (m, 1H, CH), 2.0 (s, 3H, CH_3)

IR : 1746, 1660 Cm^{-1}

BNSDOCID: <WO__03008389A1_I_>

Preparation of (S)-N-[[3-[3-Fluoro-4-[N-1[3-{(N-methyl)-N-{2-thiophenoyl (5-nitro)}] amino pyrrolidinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 91)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4-[N-1-amino pyrrolidinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide and 5-nitro-2-thiophenoic acid using Method C.

^{1}HNMR ($CDCl_3$) ppm: 7.8 (d, 1H, Ar-1H), 7.5 (d, 1H, Ar-H), 7.2 (m, 1H, Ar-H), 7.0 (d, 1H, Ar-H) 6.8 (t, 1H, Ar-H), 6.0 (t, 1H, NH), 4.70 (m, 1H, CH) 4.0 (m, 1H, CH), 3.6-3.8 (m, 8H, CH), 3.2 (broad s, 3H, CH_3), 2.5 (m, 1H, CH), 2.4 (m, 1H, CH), 2.0 (s, 3H, CH_3)

IR: 1746, 1622 cm^{-1}

Preparation of (S)-N-[[3-[3-Fluoro-4[N-1 [3-{(N-methyl)-N-2-furoyl(5-nitro)}]aminopryrolidinyl] phenyl]2-oxo-5-oxazolidinyl]methyl] acetamide. (Compound No. 92)

The title compound was prepared by reacting (S)-N-{[3-[3-Fluoro-4[N-1-aminopryrolidinyl] phenyl]2-oxo-5-oxazolidinyl]methyl] acetamide and 5-nitro-2-furoic acid using Method C.

^{1}HNMR ($CDCl_3$) ppm: 7.5 (d, 1H, Ar-H), 7.4 (m,1H, Ar-H), 7.0 (m, 2H, Ar-H), 6.8 (t, 1H, Ar-H), 6.0 (t, 1H, NH). 4.7 (m, 1H, CH), 4.0 (t, 1H, CH), 3.4-3.8 (m, 8H, CH_2), 2.6 (m, 1H, CH), 2.4 (m, 1H, CH), 2.0 (s, 1H, CH_3)

Example 15

Analogues of (S)-N-[[[3-[3-Fluoro-4-[N-1(4-N-methyl)-] aminomethyl piperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide (Core XV)

Preparation of (S)-N-[[(3-[3-Fluoro-4-[N-1[4-{N-methyl-N-2-furyl-(5-nitro)-methyl}] aminomethyl piperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide. (Compound No. 93)

The title compound was prepared by reacting (S)-N-[[(3-[3-Fluoro-4-[N-1(4-N-methyl)-] aminomethyl piperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide and5-nitro-2-furaldehyde using Method B. Synthesis of (S)-N-[[(3-[3-

BNSDOCID: <WO 03008389A1 I_>

Fluoro-4-[N-1[4--N-methyl)-] aminomethyl piperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide is similar to the synthesis of (S)-N-[[3-[3-Fluoro-4-(N-1-piperazinyl)phenyl]-2-oxo-5-oxazolidinyl]methyl-]-acetamide (Core I, US patent No. 5,700,799) except that instead of piperazine, 4-(aminomethyl)piperidine was used.

^{1}HNMR ($CDCl_3$) ppm: 7.6 (d, 1H, Ar-H), 7.5 (d, 1H, Ar-H), 7.0 (d, 1H, Ar-H), 6.9 (t, 1H, Ar-H), 6.6 (d, 1H, Ar-H), 6.0 (t, 1H, OH), 4.7 (m, 1H, CH), 4.0 (t, 1H, CH), 3.5-3.8 (m, 6H, CH), 2.8 (t, 2H, CH_2), 2.4 (m, 5N, CH_2, CH_2), 2.0 (s, 3H, CH_3), 1.8 (m, 3H, CH_2), 1.4 (m, 2H, CH_2)

Preparation of (S)-N-[[3-[3-Fluoro-4[4-N-1-4-(N-methyl) {N- 2-thiophenyl-(5-nitro)-methyl}] aminomethyl piperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide. (Compound No. 94)

The title compound was prepared by reacting (S)-N-[[3-[3-Fluoro-4[4-N-1(N-methyl)] aminomethyl piperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide and 5-nitro-2-thiophenecarboxyaldehyde using Method B.

Preparation of (s)-N-[[3-[3-Fluoro-4-{N-1[4-N-methyl)-N-2-furoyl (5-Nitro)}] aminomethyl piperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide. (Compound No. 95)

The title compound was prepared by reacting (s)-N-[[3-[3-Fluoro-4-{N-1[4-N-methyl] aminomethyl piperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide and 5-nitro-2-furoicacid using Method C.

^{1}HNMR ($CDCl_3$) ppm: 7.6 (m, 1H, Ar-H), 7.5 (m, 1H, Ar-H), 7.4 (m, 1H, Ar-H), 7.1 (d, 1H, Ar-H), 7.0 (t, 1H, Ar-H), 6.0 (t, 1H, NH), 4.7 (m, 1H, CH), 4.0 (t, 1H, CH), 3.4-3.8 (m, 10H, CH_2), 3.1 (m, 1H, CH), 2.6 (t, 2H, CH_2), 2.0 (s, 3H, CH_3), 1.6 (m, 5H, CH_2)

Preparation of (S)-N-[[3-{3-Fluoro-4-(3-oxo-piperidin-1-yl)-phenyl}-2-oxo-5-oxazolidinyl] methyl]acetamide. (Compound No. 96)

^{1}HNMR ($CDCl_3$) ppm: 7.6(d, 1H, Ar-H), 7.0 (d, 1H, Ar-H), 6.8 (m, 1H, Ar-H), 6.0 (t, 1H, NH), 4.7 (, m, 1H, CH), 4.0 (t, 1H, CH), 3.4-3.6 (m, 5H, CH_2), 3.2 (m, 2H, CH_2) 2.0 (s, 3H, CH_3), 1.9 (m, 2H, CH_2), 1.8 (m, 2H, CH_2)

BNSDOCID: <WO_03008389A1_I_>

IR : 1748, 1660

Example 16

Analogues of (S)-N[3-[3-[Fluoro-4-[N-1-[3-N-methyl]- aminopiperidinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl]acetamide (Core XVI)

Preparation of (S)-N[3-[3-[Fluoro-4-[N-1-[3-[N-methyl-N-2-furyl (5-nitro)methyl}] aminopiperidinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 97)

The title compound was prepared by reacting (S)-N[3-{3-[Fluoro-4-[N-1-[3-N-methyl]- aminopiperidinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl]acetamide (WO 95/25106) and 5-nitro-2-furaldehyde using Method B.

^{1}HNMR ($CDCl_3$) ppm: 7.6 (d, 1H, Ar-H), 7.2 (m, 1H, Ar-H), 7.0 (m, 1H, Ar-H), 6.9 (m, 1H, Ar-H), 6.6 (d, 1H, Ar-H), 6.0 (t, 1H, NH), 4.7 (m, 1H, CH), 4.0 (t, 1H, CH), 3.6-3.8 (m, 5H, CH_2) 3.2 (m, 4H, CH_2) 2.5 (s, 3H, CH_3) 2.0 (s, 3H, CH_3), 1.9 (m, 2H, CH_2) 1.8 (m, 2H, CH_2)

IR: 1749, 1659 cm^{-1}

Example 17

Analogues of (S)-N-[[3-[3-Fluoro-4-{N-1-(N-aminomethyl)-3-azabicyclo[3.1.0]-hexane]-phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide (Core XVII)

Preparation of (S)-N-[[3-[3-Fluoro-4-{N-1-(N-tert-butytloxycarbonylaminomethyl)-3-azabicyclo[3.1.0]hexane]-phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide

(a) Preparation of N-(tert-butytloxycarbonylaminomethyl)-3-azabicyclo[3.1.0]-hexane.

The title compound was prepared by following the procedure as described in US patent No. 5,164,402.

BNSDOCID: <WO 03008389A1 I >

(b) Preparation of 1-[4-(N-tert-butytloxycarbonylaminomethyl)-3-azabicyclo [3.1.0] hexane]-2-fluoro-4-nitrophenyl

To N-(tert-butytloxycarbonylaminomethyl)-3-azabicyclo[3.1.0]hexane. (A, 15g, 70.75m mol) in acetonitrile (100 mL), 3,4-difluornitrobenzene (11.24 g, 70.75m mol), and ethyldiisopropylamine (10.04 g, 77.8 m mol), were added and the reaction mixture heated to 60° C for 6 hrs. The solution was cooled to ambient temperature and concentrated to yield 22.2 g of title compound.

^{1}HNMR ($CDCl_3$) δppm: 7.9 (m, 2H), 6.89 (t, 1H), 3.4-3.8 (m,6H), 1.6 (m, 1H), 1.5 (s,9H), 0.8(m, 1H), 0.6 (m1H).

c) Preparation of 1-[4-(N-tert-butytloxycarbonylaminomethyl)-3-azabicyclo [3.1.0] hexane]-3-fluoro aniline.

To a solution of 1-[4-(N-tert-butytloxycarbonylaminomethyl)-3-azabicyclo [3.1.0] hexane]-2-fluoro-3-nitrophenyl (B, 26 g) in methanol (100 mL), 10% palladium/carbon (2.6 g) was added and shaken in a Parr hydrogenation apparatus under 40 psi of hydrogen gas for 3 hrs. Then, the reaction mixture was filtered over celite and the filtrate evaporated in vacuo to yield 24gm of the final product.

^{1}HNMR ($CDCl_3$) ppm: 6.4 – 6.8 (m,3H), 4.6 (brs, 1H,NH), 3-3.8 (m, 8H), 1.5 (s, 10H), 0.9 (m, 1H),0.6(m,1H).

d) Preparation of 1- [N- benzyloxy carbonyl-4(N-tert-butytloxycarbonyl-aminomethyl)-3-azabicyclo-[3.1.0] hexane]-3-fluoro aniline.

To a solution of 1-[4(N-tert-butytloxycarbonylaminomethyl)-3-azabicyclo [3.1.0] hexane]-3-fluoro aniline(C,24g,74.7mmols).) in

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tetrahydrofuran (200 ml) cooled to 5° C, sodium bicarbonate (25g, 298mmol) was added and then benzylchloroformate (36mL) was added dropwise. The reaction mixture was stirred for 18 hrs. at room temperature and then filtered. The filtrate was evaporated in vacuo. The residue was dissolved in ethyl acetate and washed with saturated sodium bicarbonate solution, water and brine water. The organic layer was dried over anhydrous sodium sulphate and evaporated in vacuo to give 33 g of final product.

^{1}HNMR ($CDCl_3$) δppm: 7.6 (m,5H),7.4 (m,1H), 6.8 (m, 1H), 6.6 (t,1H), 5.2(s, 2H), 4.6 (brS,1H,NH), 3.6-3.8 (m, 4H), 1.6 (m, 1H),1.5(S,9H) 0.8 (m,1H),0.6(m,1H).

e) Preparation of (R)-N[3-[3-Fluoro-4[N-1- (N-tert-butytloxycarbonylaminomethyl)-3-azabicyclo [3.1.0] hexane] phenyl-2-Oxo-5-Oxazolidinyl]methanol

To a solution of 1- [N benzyloxy carbonyl-4(N-tert-butytloxycarbonylaminomethyl)-3-azabicyclo [3.1.0] hexane]-3-fluoro aniline. (D, 25.5 g,) in dry tetrahydrofuran (150 mL), cooled to –78° C, butyl lithium(28.6mL, 15% sol. in hexane,) was added under +ve pressure of nitrogen. The reaction mixture was stirred at -78° C for 1.5 hrs. Then R-glycidyl butyrate (9.51 g) was added and the reaction mixture was stirred at -78° C for 1hr and then at room temperature for 18 hrs. To it, 100 mL of saturated ammonium chloride solution was added and the reaction mixture extracted with ethyl acetate. The combined organic layers were washed with water and brine water, dried over anhydrous sodium sulphate and evaporated in vacuo. The crude product (~28 g) was purified by column chromatography (3% MeOH/$CHCl_3$) to yield 9 g of final product.

^{1}HNMR ($CDCl_3$) ppm: 7.4 (m, 1H), 7.0 (m,1H), 6.6 (t, 1H), 4.7 (m,1H), 4.0 (m,1H), 3.8 (m, 3H), 3. 4-3.6(m, 3H),1.6(m,1H),1.5(S,9H),0.8(m,1H),0.7(m,1H).

(f) Preparation of (R)-N[3-[3-Fluoro-4[N-1- (N--tert-butytloxycarbonylamino-methyl)-3-azabicyclo [3.1.0] hexane] phenyl}-2-Oxo-5-Oxazolidinyl]methylsulfonate.

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To a solution of (S)-N[3-[3-Fluoro-4[N-1- (N-tert-butyloxycarbonylaminomethyl)-3-azabicyclo [3.1.0] hexane] phenyl-2-Oxo-5-Oxazolidinyl]methanol

(E, 1.5 g, 3.562m mol) in dichloromethane (20 mL) at 5°C, triethylamine (0.6ml, 4.275m mol) and methanesulfonylchloride (0.33ml, 4.275m mol) were added and the reaction mixture was stirred for 17 hr. Then the reaction mixture was diluted with dichloromethane and washed with saturated sodium bicarbonate solution and brine. The organic layer was dried over ahydrous sodium sulphate and evaporated in vacuo to yield 1.45 g of product.

^{1}HNMR ($CDCl_3$) ppm: 7.3 (m, 1H), 7.0 (m,1H), 6.6 (t, 1H), 4.8 (m,1H), 4.5(m2H) 4.0(t,1H), 3.9 (t,1H), 3.6-3.8 (m,2H), 3.2-3.4 (m,4H), 3.0 (S,3H), 1.6 (m,1H), 1.5 (S,9H), 0.8 (m,1H), 0.6 (m1H).

(g) Preparation of (R)-N[3-[3-Fluoro-4[N-1- (N--tert-butyloxycarbonylamino-methyl)-3-azabicyclo [3.1.0] hexane] phenyl}-2-Oxo-5-Oxazolidinyl]methylazide.

To a solution of (S)-N[3-[3-Fluoro-4[N-1- (N-tert-butyloxycarbonylaminomethyl)-3-azabicyclo [3.1.0] hexane] phenyl}-2-oxo-5-Oxazolidinyl]methylsulfonate.

(F, 1.4gm, 2.8m mol) in dimethylformamide (20 mL), sodium azide (0.547g, 8.41m mol) was added and the reaction mixture heated to 80° C for 7 hrs. The solid was filtered off and the filterate evaporated in vacuo. The residue was dissolved in chloroform and washed with water and brine solution. The organic layer was dried over anhydrous sodium sulphate and evaporated in vacuo to yield 1 g of the product.

^{1}HNMR ($CDCl_3$) ppm: 7.2 (m,1H), 7.0 (m,1H), 6.5 (t,1H), 4.8 (m,1H), 4.0 (t, 1H), 3.6-3.8 (m5H), 3.4-3.6 (m4H), 1.5 (S,9H), 1.4 (m,1H), 0.8 (m,1H), 0.6 (m,1H).

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(h) Preparation of (S)-N[3-[3-Fluoro-4[N-1- (N–tert-butytloxycarbonylamino-methyl)-3-azabicyclo [3.1.0] hexane] phenyl}-2-Oxo-5-Oxazolidinyl]methylamine..

To a solution of (S)-N[3-[3-Fluoro-4[N-1- (N-tert-butytloxycarbonylaminomethyl)-3-azabicyclo [3.1.0] hexane] phenyl]-2-Oxo-5-Oxazolidinyl]methylazide (G, 15g) in methanol (100 mL), 10% palladium/carbon (1.5 g) was added and the reaction mixture shaken in a Parr hydrogenation apparatus under 40 psi hydrogen pressure for 9 hrs. The reaction was filtered over celite and the filterate evaporated in vacuo to yield 13 g of product. The product was used as such in next step without further purification.

^{1}HNMR ($CDCl_3$) ppm: 7.2 (m, 1H), 7.0 (m, 1H), 6.6 (t,1H), 4.6 (m, 1H), 4.0 (m,1H), 3.7-3.8 (m,3H), 3.0-3.6 (m6H), 1.5 (S,10H,), 0.8 (m,1H), 0.6 (m,1H).

(i) Preparation of (S)-N[3-[3-Fluoro-4[N-1- (N-tert-butytloxycarbonylamino-methyl)-3-azabicyclo [3.1.0] hexane] phenyl}-2-Oxo-5-Oxazolidinyl]methylacetamide.

To a solution of (S)-N[3-[3-Fluoro-4[N-1- (N-tert-butytloxycarbonylaminomethyl)-3-azabicyclo[3.1.0] hexane] phenyl}-2-Oxo-5-Oxazolidinyl]methylamine (H, 14 g, 33.5m mol) in dichloromethane (150 mL), triethylamine (6.98ml) and acetic anhydride (4.12ml) were added and the reaction mixture was stirred at room temperature for 17 hrs. Then the reaction mixture was diluted with dichloromethane and washed with saturated sodium bicarbonate solution and brine water. The organic layer was dried over anhydrous sodium sulphate and evaporated in vacuo. The residue was purified by column chromatography to yield 10 g of final product.

^{1}HNMR ($CDCl_3$) ppm: 7.4 (m, 1H), 7.0 (m, 1H), 6.0 (m, 1H), 4.7 (m, 1H), 4.65 (br s, 1H), 4.06 (t, 1H), 3.5-3.7 (m, 5 H), 3.0-3.5(m,4H), 2.0 (s,3H), 1.5 (s, 10H), 0.8 (m, 1H), 0.67 (m, 1H).

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(j) (S)-N[3-[3Fluoro-4[N-1- (aminomethyl)-3-azabicyclo [3.1.0] hexane] of phenyl}-2-Oxo-5-Oxazolidinyl]methylacetamide.

To a solution of (S)-N[3-[3-Fluoro-4[N-1- (N-tert-butytloxycarbonylamino-methyl)-3-azabicyclo [3.1.0] hexane] phenyl}-2-Oxo-5-Oxazolidinyl]methylacetamide (I, 0.5g,) in dichloromethane (8 mL), trifluoroacetic acid (2 mL) was added and stirred for 2 hrs. Then the reaction mixture was evaporated and dried in vacuo. To the residue in acetone (10 mL), potassium carbonate (0.78 g, 5.55 mmol) was added and stirred for 15 minutes. Then the reaction mixture was fitered and the filterate evaporated in vacuo to yield the product in quantitative yield. This product was used as such in next step without further characterization.

Preparation of (S)-N-[[3-[3-Fluoro-4[N-1-[3-{2-furyl-(5-nitro)-methylene}aminomethyl]-3-azabiyclo (3.1.0)hexane]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide. (Compound No. 98)

The tittle compound was prepared with (S)-N[3-[3-Fluoro-4[N-1-(aminomethyl)-3-azabicyclo [3.1.0] hexane] of phenyl}-2-oxo-5-oxazolidinyl]methylacetamide and 5-nitro-2-furaldehyde.

^{1}HNMR ($CDCl_3$) ppm: 8.2 (s, 1H, CH), 7.4 (m, 2H, Ar-H), 7.0 (m, 2H, Ar-H), 6.4 (m, 1H, Ar-H), 6.0 (t, 1H, NH), 4.7 (m, 1H, CH), 3.4-3.8 (m, 1H, CH_2), 2.0 (s, 3H, CH_3), 1.6 (m, 1H, CH), 0.8 (m, 1H, CH), 0.6 (m, 1H, CH)

IR: 1745, 1659 cm^{-1}

Preparation of (S)-N-[[3-[3-Fluoro-4[N-1[3-{N-2-furyl-(5-nitro)methyl}-aminomethyl]-3-azabicyclo[3.1.0]hexane]phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide. (Compound No. 94)

The title compound was prepared with (S)-N[3-[3-Fluoro-4[N-1-(aminomethyl)-3-azabicyclo [3.1.0] hexane] phenyl}-2-oxo-5-oxazolidinyl]methylacetamide and 5-nitro-2-furaldehyde using Method B.

^{1}HNMR ($CDCl_3$) ppm: 7.4 (m, 2H, Ar-H), 7.0 (d, 1H, Ar-H), 6.7 (t, 1H, Ar-H), 6.5 (d, 1H, Ar-H), 6.0 (t, 1H, NH), 4.7 (m, 1H, CH), 3.4-4.0 (m, 8H, CH_2) 3.2 (m, 2H, CH_2) 3.0 (d, 2H, CH), 2.8 (d, 1H, CH_2) 2.0 (s, 3H, CH_3) 1.4 (m, 1H, CH), 0.8 (m, 1H, CH), 0.6 (m, 1H, CH).

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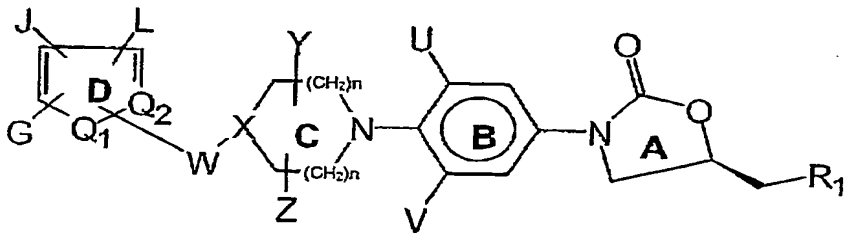
CLAIMS:

1. A compound having the structure of Formula I,



Formula I

and its pharmaceutically acceptable salts, enantiomers, diastereomers, N-oxide, polymorphs, pharmaceutically acceptable solvates, prodrugs or metabolites, wherein

ring D is a five membered heterocyclic ring;

ring C is four to eight membered in size or larger which has either two or three carbon atoms between each nitrogen atoms or ring C is a bridged bicyclic system and is optionally substituted by the substituents Y and Z independently selected from alkyl groups, cycloakyl groups, fluoro group, carboxylic groups and corresponding esters or amides;

Q_1 is selected from O, S, NR_{11};

Q_2 is selected from N or C;

G, J, L are independently selected from H, C_{1-6} alkyl, F, Cl, Br,I, –CN, COR_5,$COOR_5$, $N(R_6,R_7)$, $NHCOC(R_5, R_8, R_9)$,-$NHCOOR_5$,CON (R_6, R_7), CH_2NO_2, NO_2, CH_2R_8, CHR_9, -CH = N-OR_{10}, -C=CH-R_5, OR_5, SR_5, -$C(R_9)=C(R_9)NO_2$, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I, OR_4, SR_4; wherein R_5 is selected from H, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted with one or more of F, Cl, Br, I or OH, aryl, heteroaryl; R_6 and R_7, are independently selected from H, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy; R_8 and R_9 are independently selected from H, C_{1-6} alkyl, F, Cl, Br, I, C_{1-12} alkyl substituted

with one or more of F, Cl, Br, I, OR_5, SR_5, $N(R_6,R_7)$; R_{10}= H, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, aryl, heteroaryl; except when W is C=O, Q_1=S, Q_2= C, and G, J, L=H;

R_1 is selected from the group consisting of - $NHC(=O)R_2$, $N(R_3, R_4)$, $-NR_2C(=S)R_3$, $-NR_2C(=S)SR_3$, wherein R_2 is hydrogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted with one or more of F, Cl, Br, I or OH; R_3,R_4 are independently selected from hydrogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted with one or more of F, Cl, Br, I or OH;

U and V are independently selected from hydrogen, optionally substituted C_{1-6} alkyl, F, Cl, Br, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I;

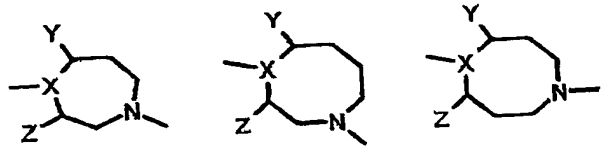
X is selected from C, CH, CH-S, CH-O and N;

Y and Z are independently selected from hydrogen, C_{1-6} alkyl, C_{3-12} cycloalkyl and C_{0-3} bridging groups;

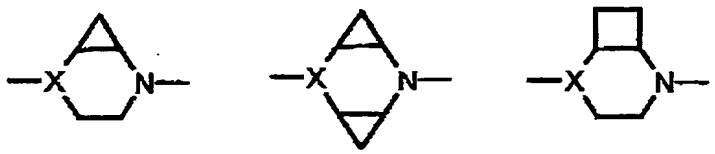
W is selected from the group CH_2, CO, CH_2NH, $-NHCH_2$, $-CH_2NHCH_2$, $-CH_2-N(R_{11})$ CH_2 -, CH_2 (R_{11}) N -, CH (R_{11}), S, CH_2(CO), NH, O, $N(R_{11})$, $(CO)CH_2$, $N(R_{11})CON(R_{11})$, $N(R_{11})C(=S)N(R_{11})$, SO_2, SO, wherein R_{11} is hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl, heteroaryl;

n is an integer ranging from 0 to 3.

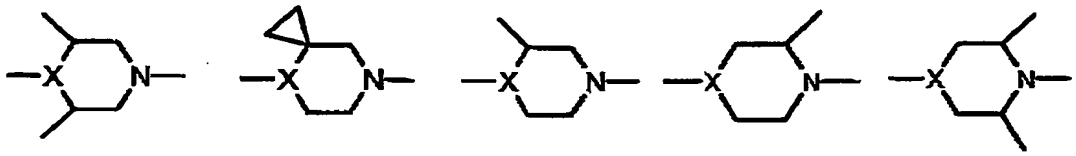
2. The compound of Formula I according to claim 1 wherein ring C is four to eight membered in size or the larger size which have either two or three carbon atoms between each nitrogen atom, comprising of



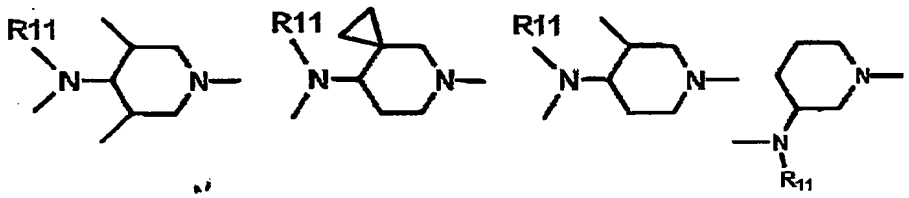
or ring C is bridged to form a bicyclic system as shown below,

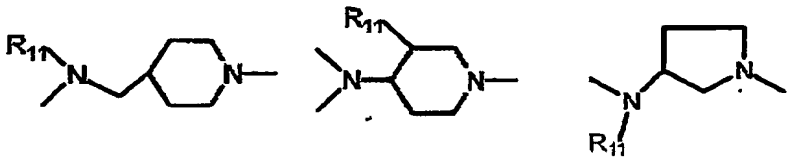


ring C is optionally substituted by Y and Z, independently selected from alkyl groups, cycloalkyl groups, fluoro group, carboxylic and corresponding esters, amides, substituted alkyls or bridging alkyl groups which are as shown below:



the five or six membered ring C (when X is -CH-(NHR), or $>CCH_2(NHR-)$ is selected from the group consisting of the following rings,





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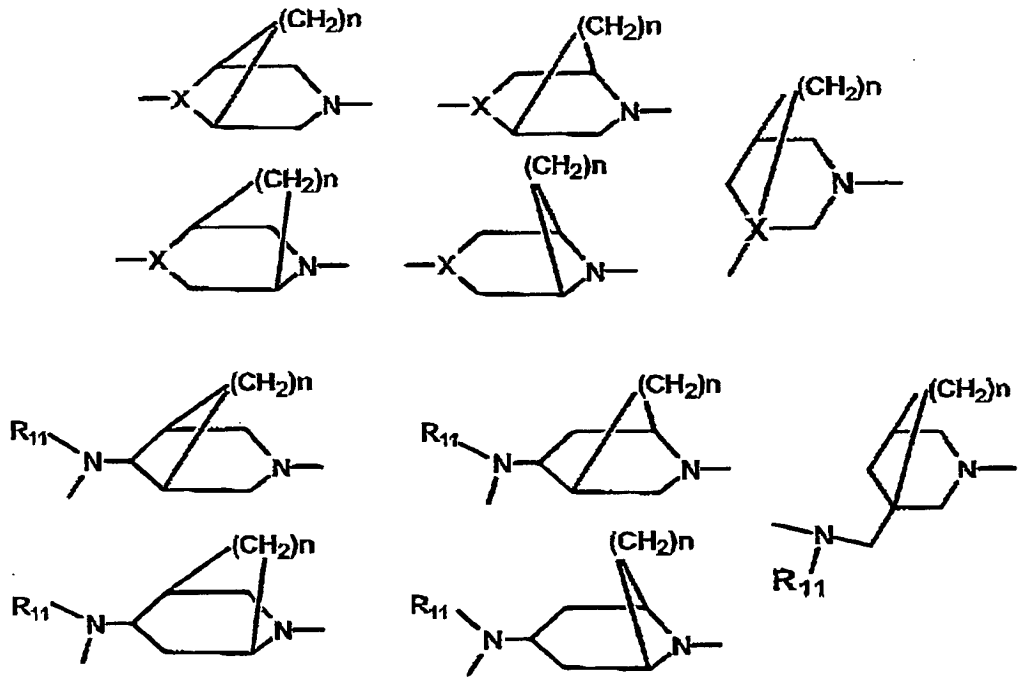
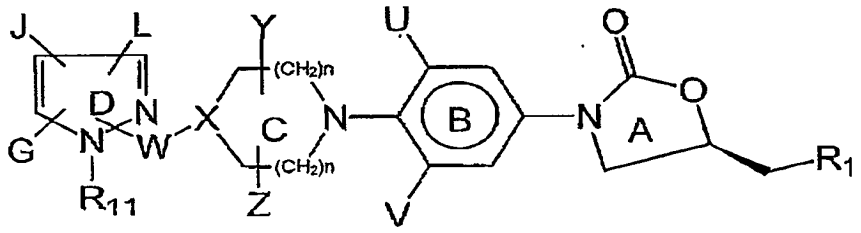
and the bicyclic bridged ring C is selected from the group consisting of the following rings,



3. The compound of Formula I according to claim1 wherein ring D is selected from the group consisting of furanyl, thienyl, pyrrolyl and pyrazolyl.

4. The compound of Formula I according to claim 1 wherein Q_1 = NR_{11} and Q_2 = N shown as Formula II below

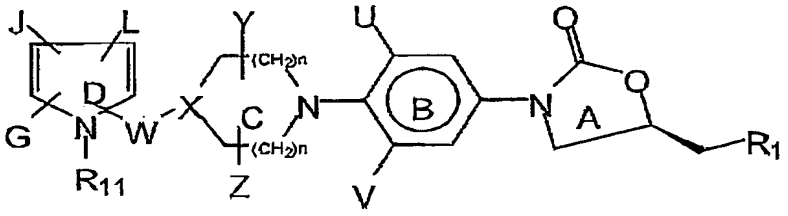


Formula II

5. The compund of Formula II according to claim 4 selected from the group consisting of:

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-pyrazolecarbonyl-(4-nitro)}]piperazinyl] phenyl-]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-pyrazolecarbonyl-(5-nitro)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide.

6. The compound of Formula I according to claim 1 wherein Q_1 = NR_{11} and Q_2 = C shown as Formula III below,

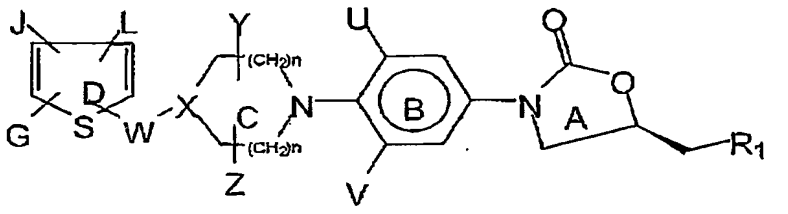


Formula III

7. The compound of Formula III according to claim 6 selected from the group consisting of:

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-pyrrole-(1-methyl-5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl] acetamide.
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-pyrrole-(5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl] acetamide

8. The compound of Formula I according to claim 1 wherein Q_1=S and Q_2=C shown as Formula IV below,



Formula IV

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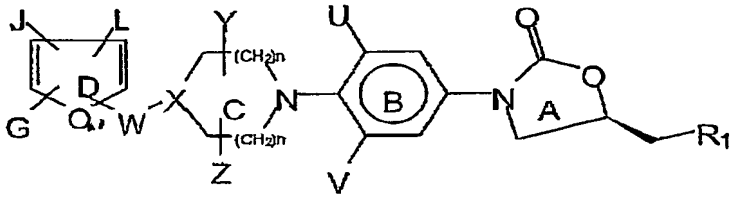
9. The compound of Formula IV according to claim 8 selected from the group consisting of:

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen-(4-nitro-)methyl-}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(5-nitro)}] homopiperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-[1-{2-thiophenyl-(5-nitro)}-1-ethyl]]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[2-methyl-4-{2-thiophenoyl-(5-nitro)}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-2-thiohenoyl-(5-nitro)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1, {3-{[N-methyl) [N-{2-thiophenoyl (5-nitro)}] amino pyrrolidinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

10. The compound of Formula I according to claim 1 wherein Q_1=O and Q_2=C shown as Formula V below,



Formula V

11. The compound of Formula V according to claim 10 selected from the group consisting of:

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl-(3-methyl)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl-(3-methyl-5-nitro)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-[1-{2-furyl-(5-nitro)}-1-ethyl]]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-difluoroacetamide,
- (S)-N-[[3-[3-Fluoro-4-[4-{N-2-furyl-(5-nitro)methyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide

12. A compound selected from the group consisting of:

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-(2-furyl-carbonylmethyl)]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-(2-thiophenoyl-methyl)]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl{5-(4-chloro-2-nitro-)-phenyl}methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen-(4-bromo-5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl-(3-methyl-5-nitro)methyl-}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-cyano-5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-(4-chloro)phenyl)methyl}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl],
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-furyl(5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-(4-bromo)phenyl)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-methyl)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-pyrrole-(1-methyl-4-nitro) methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-pyrrole-(1-methyl-5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-pyrrole-(5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl] acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen-(4-nitro-)methyl-}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl-(5-methoxy)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,
- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-[2-furyl-{5-O-(2-nitro-4-fluoro-phenyloxy)} methyl]]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

BNSDOCID: <WO_03008389A1 I >

- (S)-N-[[3-[3-Fluoro-4-[N-1[4-{2-furyl (5-chloro)methyl}] piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1 [4-{3-furyl(2-nitro)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen-(4-dimethylamino-5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-morpholino-5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl-(5-methylsulphonyl-)methyl-}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-(4-nitro)-phenyl)-methyl}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-(3-nitro-)phenyl-)methyl}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-(2-nitro)-phenyl)-methyl}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4[N-1-[4-{2-Furyl-4-bromo-(5-nitro)methyl}]piperazinyl]-phenyl]-2-oxo-5-oxazolidinyl]methl]acetamide,

- (S)-N-[[3-[3-Fluoro-4[N-1-[4-{2-Furyl-(4-isopropyl)methyl}]piperazinyl]-phenyl]-2-oxo-5-oxazolidinyl]methl]acetamide,

- (S)-N-[[3-[3-Fluoro-4[N-1-[4-{2-Furyl-4-isopropyl(5-nitro)methyl}] piperazinyl]-phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl(5-methoxy)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(5-acetamido)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-pyrazolecarbonyl-(4-nitro)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-pyrazolecarbonyl(5-nitro)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(5-tert-butoxy-carboxamido)}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl] acetamide,

BNSDOCID: <WO 03008389A1 I >

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl(5-trifluoroacetamido)}] piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl],

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl(5-amino)}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl{5-(4-chloro-2-nitro-)-phenyl}}] piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl],

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl-(3-methyl)}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl-(3-methyl-5-nitro)}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(4-dimethylamino-5-nitro)}] piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-Furoyl–(5-nitro)acrylic}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl–(5-nitro)acrylic}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,

- Iodide (S)-N-[[3-[3-Fluoro-4-[N-1-[4-N-methyl-4-{2-furyl-(5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl] methyl] acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-nitro)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-fluoroacetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen(5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]fluoroacetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophen(5-nitro)methyl}]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]difluoroacetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-nitro)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-difluoroacetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-nitro)methyl}]piperazinyl]phenyl]]-2-oxo-5-oxazolidinyl]methyl]mono chloro acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1[4-[2-thiophenyl-5-nitro)methyl}],

- (S)-N-[[3-[3-Fluoro-4-[N-1 [4-[2-thiophenyl-4bromo-(5-nitro)methyl}] piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl] monochloroacetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1 [4-[2-thiophenyl–(5-nitro)methyl}]piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl]–2-chloropropionamide,

BNSDOCID: <WO_03008389A1_I_>

- (S)-N-[[3-[3-Fluoro-4-[N-1 [4-[2-Furyl–(5-nitro)methyl}]piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl] –2-chloropropionamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1 [4-[2-thiophenyl-4-bromo-(5-nitro)methyl}] piperazinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl]–2-chloropropionamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furyl(5-nitro)methyl}]homopiperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-{4-(3-furoyl)}homopiperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophenoyl-(5-nitro)}]homopiperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-furoyl(5-nitro)}]homopiperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-{2-methyl-4-(t-butoxycarbonyl)}piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2-methyl-4-{2-thiophen-(5-nitro)methyl}] piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2-methyl-4-{2-furyl(5-nitro)methyl}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2-methyl-4-{2-furoyl-(5-nitro)}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2-methyl-4-{2-thiophenoyl-(5-nitro)}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furoyl-}]-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(5-formyl)methyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(5-nitro)methyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(5-hydroxymethyl) methyl-}]-piperazinyl]phenyl]-2-oxo-5 oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(aldoxime)methyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-(2-thienylacetyl)]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

PNISDOCID: <WO 03008389A1 >

- (S)-N-[[3-[3-Fluoro-4-[N-1-[2,6-dimethyl-4-{2-furyl-(5-cyano)methyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[3-methyl-4-{2-thienylacetyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[3-methyl-4-{2-furoyl-(5-nitro)}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[3-methyl-4-{2-thienoyl-(5-nitro)}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{3-methyl-2-furyl-(5-formyl)methyl-}]-piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[4-{N-acetyl-N-2-furyl-(5-nitro)methyl-}]amino piperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[{3-methyl-4-(N-methyl-N-thiophenacetyl-)}-amino piperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[[3-methyl-4-{N-methyl-2-furoyl(5-nitro)}]-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[[3-methyl-4-{N-methyl-2-thienoyl-(5-nitro)}]-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[{3-methyl-4-(N-methyl-N-2-furoyl)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[[3-methyl-4-{N-methyl-N-2-furyl(5-nitro)}]-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[[3-methyl-4-{N-methyl-N-2-thienyl-(5-nitro)}]-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-2-thienoyl-(5-nitro)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-2-furoyl-(5-nitro)}aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-N-2-furoyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-N-2-thiophenacetyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

BNSDOCID: <WO__03008389A1_I_>

- (S)-N-[[3-[3-Fluoro-4-[4-{N-ethyl-N-2-thiophenyl-(5-nitro)methyl}-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[4-{N-thienyl-(5-nitro)methyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[4-{2-furyl-(5-nitro)methylene}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[4-{N-2-furyl-(5-nitro)methyl}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[4-{N-methyl-N-2-pyrrole-(5-nitro)methyl}-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[4-{N-methyl-N-2-furyl-(5-acetoxymethyl)methyl}-aminopiperidine-1-yl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[4-{N-methyl-N-2-furoyl-(5-nitro)}-aminopiperidine-1-yl] phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4[N-1,3-[N-methyl[N-{2-thiophenyl(5-nitro)methyl}] aminopyrodinyl]phenyl]]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1, {3-{[N-methyl) [N-{2-thiophenoyl (5-nitro)}] amino pyrrolidinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-{[3-[3-Fluoro-4[N-1[3-{(N-methyl)[N-2-furoyl(5-nitro)}] aminopryrolidinyl]phenyl]2-oxo-5-oxazolidinyl]methyl]acetamide.,

- (S)-N-[[(3-[3-Fluoro-4-[N-1[4-{N-methyl)-N-2-furyl-(5-nitro)-methyl}] aminomethylpiperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide,

- (S)-N-[[3-[3-Fluoro-4[4-N-1(N-methyl){N-2-thiophenyl-(5-nitro)-methyl}] aminomethylpiperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide,

- (S)-N-[[3-[3-Fluoro-4-{N-1[4-N-methyl)-N-2-furoyl(5-Nitro)-methyl}] aminomethylpiperidine-1-yl]-phenyl]-2-oxo-5-oxazolidinyl]methyl] acetamide,

- (S)-N-[[3-{3-Fluoro-4-(3-oxo-piperidin-1-yl)-phenyl}-2-oxo-5-oxazolidinyl] methyl]acetamide,

- (S)-N[3-{3-[Fluoro-4-[N-1-[3-N-methyl]-N-2-furyl (5-nitro)methyl}] amino piperidinyl]-phenyl]2-oxo-5-oxazolidinyl]methyl]acetamidezolidinyl] methyl]acetamide,

BNSDOCID: <WO__03008389A1_I_>

- (S)-N-[[3-[3-Fluoro-4[N-1-[3-{2-furyl-(5-nitro)-methylene}aminomethyl]-3-azabiyclo(3.1.0)hexane]phenyl]-2-oxo-5-oxazolidinyl]methyl]acetamide,

- (S)-N-[[3-[3-Fluoro-4[N-1[3-{N-2-furyl-(5-nitro)methyl}-aminomethyl]-3-azabicyclo[3.1.0]hexane]phenyl]-2-oxo-5-oxazolidinyl] methyl] acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-[1-{2-thiophenyl-(5-nitro)}-1-ethyl]]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-[1-{2-furyl-(5-nitro)}-1-ethyl]]piperazinyl] phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-(4-t-butoxycarbonyl) piperazinyl-5-nitro)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl] methyl]-acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-N-piperazinyl-5-nitro)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,

- (S)-N-[[3-[3-Fluoro-4-[N-1-[4-{2-thiophene-(4-(4-methyl)piperazinyl-5-nitro)methyl}]piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-acetamide,

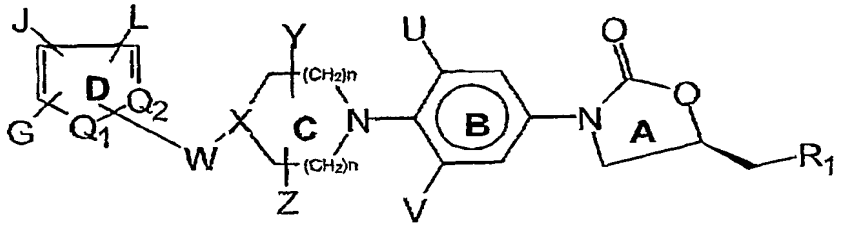
13. A pharmaceutical composition comprising the compound of claim 1 or 12 and a pharmaceutical acceptable carrier, diluent, excipient or solvate.

14. A pharmaceutical composition comprising a pharmaceutically effective amount of a compound according to claims 1 or 12, or a physiologically acceptable acid additional salt thereof with a pharmaceutically acceptable carrier for treating microbial infections.

15. A method of treating or preventing microbial infection in a mammal comprising administering to said mammal the pharmaceutical composition according to claim 14.

BNSDOCID: <WO 03008389A1 I >

16. A process for preparing a compound of Formula I,



Formula I

and its pharmaceutically acceptable salts, enantiomers, diastereomers, N-oxide, polymorphs, pharmaceutically acceptable solvates prodrugs or metabolites, wherein

ring D is a five membered heterocyclic ring;

ring C is four to eight membered in size or larger which has either two or three carbon atoms between each nitrogen atoms or ring C is a bridged bicyclic system and is optionally substituted by the substients Y and Z independently selected from alkyl groups, cycloakyl groups, fluoro group, carboxylic groups and corresponding esters or amides;

Q_1 is selected from O, S, NR_{11};

Q_2 is selected from N or C;

G, J, L are independently selected from H, C_{1-6} alkyl, F, Cl, Br,I, –CN, COR_5,$COOR_5$, $N(R_6,R_7)$, $NHCOC(R_5, R_8, R_9)$,-$NHCOOR_5$,CON (R_6, R_7), CH_2NO_2, NO_2, CH_2R_8, CHR_9, -CH = N-OR_{10}, -C=CH-R_5, OR_5, SR_5, -$C(R_9)$=$C(R_9)NO_2$, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I, OR_4, SR_4; wherein R_5 is selected from H, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted with one or more of F, Cl, Br, I or OH, aryl, heteroaryl; R_6 and R_7 are independently selected from H, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy; R_8 and R_9 are independently selected from H, C_{1-6} alkyl, F, Cl, Br, I, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I, OR_5, SR_5, $N(R_6,R_7)$; R_{10}= H, optionally substituted

PNSDOCID: -WO 03008389A1 I >

C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, aryl, heteroaryl; except when W is C=O, Q_1=S, Q_2= C, and G, J, L=H;

R_1 is selected from the group consisting of - $NHC(=O)R_2$, $N(R_3, R_4)$, $-NR_2C(=S)R_3$, $-NR_2C(=S)SR_3$, wherein R_2 is hydrogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted with one or more of F, Cl, Br, I or OH; R_3,R_4 are independently selected from hydrogen, C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl substituted with one or more of F, Cl, Br, I or OH;

U and V are independently selected from hydrogen, optionally substituted C_{1-6} alkyl, F, Cl, Br, C_{1-12} alkyl substituted with one or more of F, Cl, Br, I;

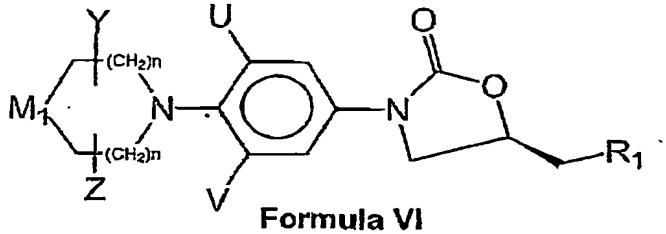
X is selected from C, CH, CH-S, CH-O and N;

Y and Z are independently selected from hydrogen, C_{1-6} alkyl, C_{3-12} cycloalkyl and C_{0-3} bridging groups;

W is selected from the group CH_2, CO, CH_2NH, $-NHCH_2$, $-CH_2NHCH_2$, $-CH_2-N(R_{11})CH_2-$, $CH_2(R_{11})N-$, $CH(R_{11})$, S, $CH_2(CO)$, NH, O, $N(R_{11})$, $(CO)CH_2$, $N(R_{11})CON(R_{11})$, $N(R_{11})C(=S)N(R_{11})$, SO_2, SO, wherein R_{11} is hydrogen, optionally substituted C_{1-12} alkyl, C_{3-12} cycloalkyl, C_{1-6} alkoxy, C_{1-6} alkyl, C_{1-6} alkylcarbonyl, C_{1-6} alkylcarboxy, aryl, heteroaryl;

n is an integer ranging from 0 to 3;

which comprises reacting an amine compound of Formula VI



Formula VI

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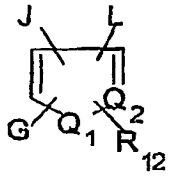
with a heterocyclic compound of Formula VII



Formula VII

wherein Q_1, Q_2, G, J, L, W, X Y, Z, U, V, R_1 and n are the same as defined above and M_1 in amine of Formula VI is defined as NH, $CH(NHR_{13})$, $-CH-CH_2NHR_{13}$, CCH_2NHR_{13} wherein R_{13} is H, methyl , ethyl, isopropyl, acetyl, cyclopropyl, alkoxy or acetyl;

R_{12} is a suitable leaving group or suitable functional group.

17. The process according to claim 16 wherein the suitable leaving group R_{12} is selected from the group comprising of fluoro alkyl, chloro alkyl, bromo alkyl SCH_3, $-SO_2CH_3$,$-SO_2CF_3$ and OC_6H_5.

18. The process according to claim 16 wherein the suitable functional group is carboxaldehyde or carboxylic acid.

19. The process according to claim 16 for preparing a compound of Formula I wherein reaction of compounds of Formula VI and VII is carried out in a suitable solvent selected from the group consisting of N,N-dimethylformamide, dimethylacetamide, dimethylsulfoxide, ethanol and ethylene glycol.

20. The process according to claim 19 wherein the reaction is carried out in the presence of a base selected from the group consisting of triethylamine, diisopropylamine, potassium carbonate and sodium carbonate.

21. The process according to claim 16 for preparing a compound of Formula I wherein a compound of Formula VII is a heterocyclic aldehyde.

22. The process according to claim 16 wherein the reductive amination of the compound of Formula VI with the heterocyclic aldehyde of Formula VII is

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performed with a reducing agent selected from the group consisting of sodium triacetoxyborohydride and sodium cyanoborohydride to give a compound of Formula I wherein W=CH_2.

23. The process according to claim 16 wherein the compound of Formula VII is a heterocyclic carboxylic acid.

24. The process according to claim 16 wherein the reaction of amine of Formula VI with carboxylic acid of Formula VII is carried out in the presence of a suitable condensing agent.

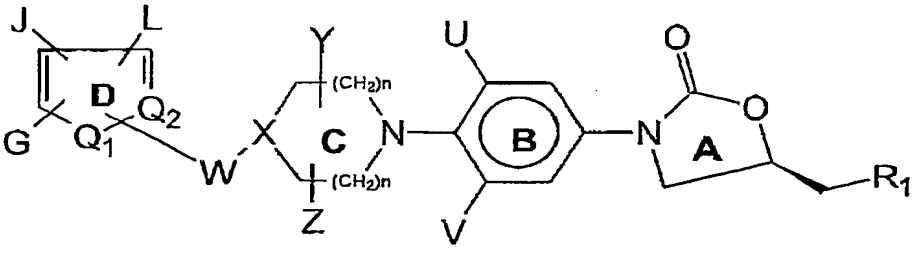
25. The process according to claim 24 wherein the suitable condensing agent is selected from the group consisting of 1,3-dicyclohexylcarbodiimide (DCC) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC).

26. The process according to claim 16 for preparing a compound of Formula I wherein the compounds of Formula I having carbonyl link are prepared by reacting heteroaromatic compound of Formula VII with a compound of Formula VI in the presence of triphosgene and phosgene.

27. The process according to claim 22 wherein compound of Formula VII is N-methyl pyrrole.

28. The process according to claim 16 for preparing a compound of Formua I wherein W=CO comprising reacting 3-bromothiophene (Formula VII) and amine of Formula VI with carbon monoxide.

29. The process according to claim 16 for preparing a compound of Formula I



Formula I

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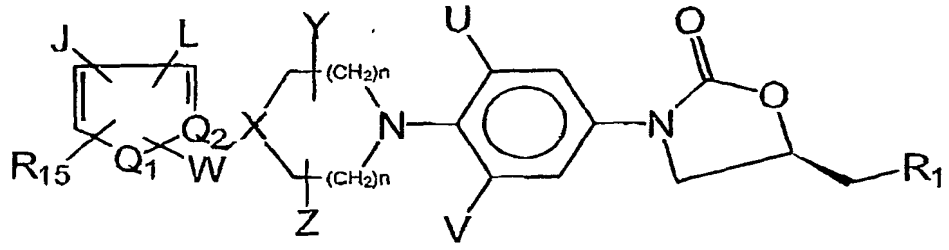
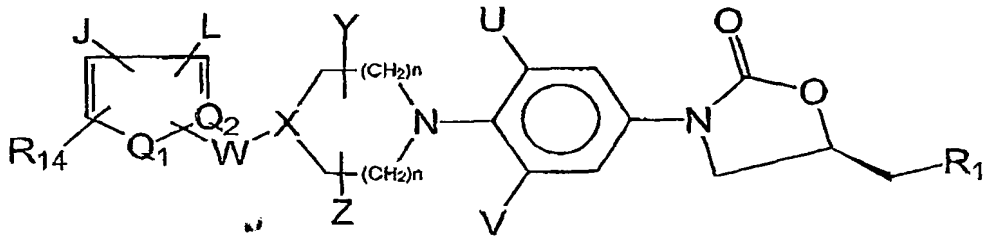
when G=R_{15} shown as Formula IX



Formula IX

wherein R_{15} is a subset of G comprising of amine and acetamide,

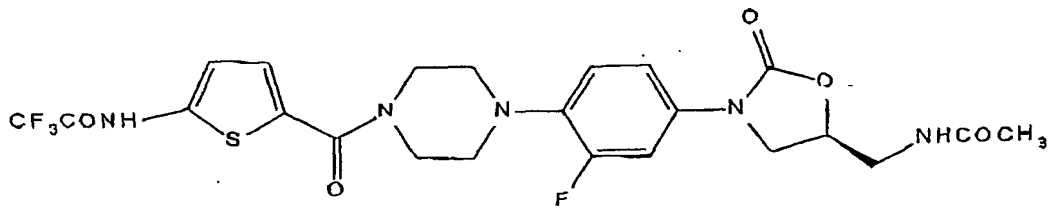
comprising converting compound of Formula VIII (Formula I, when G=R_{14} wherein $R=_{14}$ is also a subset of G comprising carbamate)



Formula VIII

to a compound of Formula IX (Formula I, when G=R_{15}).

30. The process according to claim 16 for preparing a compound of Formula I when G=NHCOCF$_3$, Q_1=S, Q_2=C, G=J=L=H, W=CO, X=N, Y=Z=H, n=1, U=H, V=F, R1=NHCOCH$_3$) shown as Formula XI



FORMULA XI

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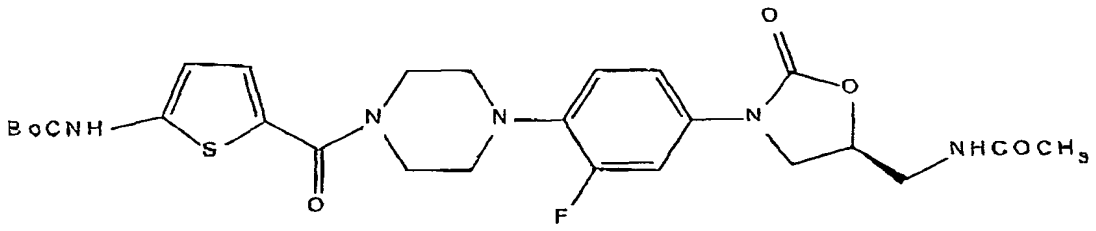
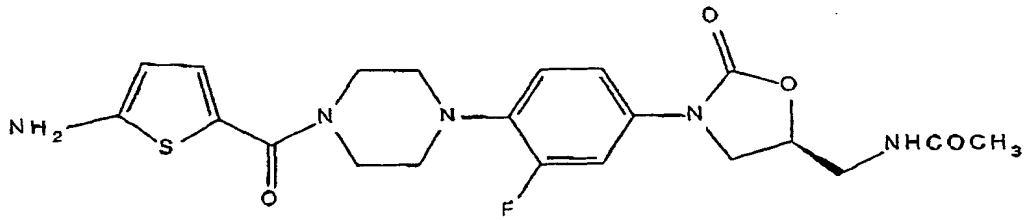
comprising reacting compound of Formula X with trifluoroacetic acid.



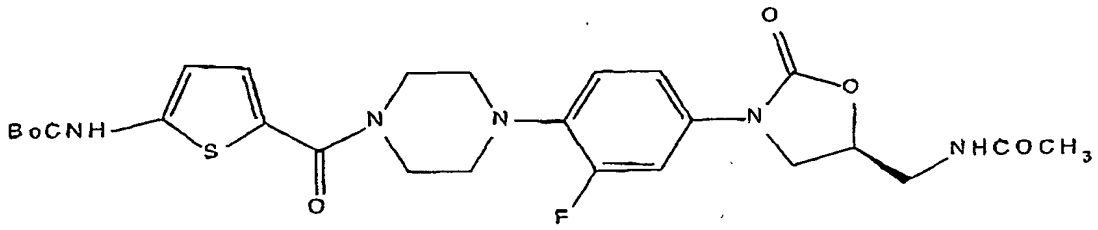
FORMULA X

31. The process according to claim 16 for preparing a compound of Formula I when G=NH_2, Q_1=S, Q_2=C, G=J=L=H, W=CO, X=N, Y=Z=H, n=1, U=H, V=F, R1=$NHCOCH_3$) shown as Formula XII



FORMULA XII

comprising reacting compound of Formula X



FORMULA X

with trifluoroacetic acid followed by potassium carbonate in a suitable solvent.

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB02/00167

A. CLASSIFICATION OF SUBJECT MATTER
IPC(7) : C07D 241/02, 243/08, 263/04, 413/14; A61K 31/55, 31/535, 31/495, 31/50, 31/445, 31/42; A61P 31/00
US CL : 514/218, 235.8, 252.11, 254.02, 254.04, 326, 376; 540/575; 544/121, 357, 369; 546/209; 548/229, 231, 232
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
U.S. : 514/218, 235.8, 252.11, 254.02, 254.04, 326, 376; 540/575; 544/121, 357, 369; 546/209; 548/229, 231, 232

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
CAS ONLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P	WO 02/06278 A1 (RANBAXY LABORATORIES LIMITED) 24 January 2002, see entire document.	1-31
X	PAE et al., Synthesis and in vitro Activity of New Oxazolidinone Antibacterial Agents Having Substituted Isoxazoles, Bioorganic & Medicinal Chemistry Letters, 20 September 1999, Vol. 9, No. 18, pages 2679-2684, especially page 2681.	1, 2, 13-16, 18 and 21-23
X	PAE et al., 3D QSAR Studies on New Oxazolidinone Antibacterial Agents By Comparative Molecular Field Analysis, Bioorganic & Medicinal Chemistry Letters, 20 September 1999, Vol. 9, No. 18, pages 2684-2690, especially page 2688.	1, 2 and 13-15

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Date of the actual completion of the international search	Date of mailing of the international search report
12 July 2002 (12.07.2002)	20 AUG 2002
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703)305-3230	Authorized officer Brenda L. Coleman Telephone No. 703-308-1235

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